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PRESIDENTIAL ADDRESS

THE ROAD AHEAD FOR THORACIC SURGERY

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MEMBERS of The American Association for Thoracic Surgery: I am deeply appreciative of the honor conferred by you in electing me President of this young Association. I say "young" advisedly. Thoracic surgery was in an embryonic state when this Association was founded in 1917. Today thoracic surgery is in its youth and has not yet attained maturity. My own professional life has spanned the last 34 of the 44 years that this Association has been in existence. In these 34 years the surgery for pulmonary tuberculosis has shifted from collapse to excisional therapy. Thirty-four years ago a one-stage pneumonectomy was unheard of, and lobectomies were performed crudely, using a tourniquet. After the pioneering work of our former presidents, Graham[16] and Blades,[3] one-stage pneumonectomies and lobectomies are performed at the present time with precision and individual handling of the arteries, veins, and bronchi leading to the lung or lobe.

Twenty-three years ago, the first successful resection of the esophagus for cancer with restoration of continuity of the gastrointestinal tract was reported by a former president, Adams, and Phemister.[1] Five years later, a former president, Haight,[19] reported the successful treatment of congenital atresia of the esophagus by immediate restoration of continuity rather than with a gastrostomy and a mucous fistula in the neck. Today the entire esophagus can be removed and replaced with another organ within the chest, joining the

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pharynx to the stomach, so that patients may eat normally. The surgical treatment of œsophageal hiatal hernia is now a routine operation, thanks to the pioneering efforts of a former president of this Association, Harrington, and the work of our Honorary Member from England, Mr. Philip Allison.

Thirty-three years ago, our former president, Churchill,[5] performed the first successful pericardectomy for Pick's disease. At that time, the only operations performed on the heart or the pericardium were the drainage of pus from the pericardial sac and the suturing of stab wounds, aside from the early attempts to open stenotic mitral valves by Cutler, Levine, and our former president Beck.[8]

Operations on the thoracic aorta began with the first successful ligation of a patent ductus by Gross[17] in 1939 and the excision and restoration of continuity of the aorta in patients with coaretation in 1945 by Crafoord,[7] our Honorary Member from Sweden, and by Gross.[18] These operations are now commonplace. Great strides have also been taken in the replacement of the diseased aorta, including even the arch itself, first with homografts and then with prostheses of plastic materials. Our former president De Bakey has made monumental contributions in this field.[9]

A great step forward in the treatment of cyanotic congenital cardiac disease was taken 16 years ago by a former president, Blalock, and Taussig[4] when they reported the alleviation of the symptoms of the tetralogy of Fallot by the anastomosis of a systemic artery to a pulmonary artery. Operations within the heart were pioneered by Harken[20] in 1948 and Bailey[2] in 1949 with the successful opening of stenotic mitral valves. During the next 7 years, many ingenious methods were devised to operate within the heart by the sense of touch, without being able to see the structure being operated upon. An improvement occurred when the body temperature of patients was lowered sufficiently to permit the interruption of the flow of blood through the heart and lungs for as long as 4 to 8 minutes.[24] During this brief interval, the empty chambers of the heart could be opened and the structure operated upon could be seen. Cross circulation between the patient and a suitable donor[21] was also used for the same purpose until better and safer methods of opening the heart became available.

Eight years ago, your president was fortunate enough to operate successfully within the heart under direct vision and to close a large atrial septal defect.[14] This was accomplished by using an extracorporeal circulation which temporarily took over the function of the heart and lungs. The development of this extracorporeal circulation was begun in 1934, and its successful use in animals was reported in 1937 and 1939.[12, 13] At present, prolonged delicate operations within the opened chambers of the heart are performed all over the world, using either an extracorporeal circulation to bypass the heart and lungs, or hypothermia, or a combination of the two. The surgical conquest of the heart has been achieved.

This brief review of some of the highlights in our field of surgery necessarily skips over much important work. These achievements of thoracic surgery would have been impossible without many concurrent developments in other fields.

The availability of heparin some 25 years ago opened the way for the development of the extracorporeal circulation. First sulfonamides and then antibiotics have aided in eliminating the crippling empyemas which so commonly occurred when thoracic surgery was in its infancy. Improvement in anesthetic techniques and an increasing and more widespread knowledge of cardiopulmonary physiology has enable many patients to survive operations which formerly were attended with a forbidding mortality.

And so thoracic surgery stands at the threshold of manhood. Much has been accomplished, yet much remains to be done. As Tennyson said: "Some work of noble note may yet be done."[26] We must inevitably move forward. We can no longer accept our pioneering mortality. We must increase the safety of the formidable operations we now perform within the thorax. We still know little more than our forebears about the nature of achalasia of the esophagus. We are beginning to treat that crippling respiratory disease, emphysema, by surgical methods. We have made little if any progress in improving the blood flow to an hypoxic myocardium. This problem must and will be solved. We have made a start in replacing deformed and diseased valves of the heart with artificial valves. We have also made a start in providing artificial pacemakers for the heart in a number of disease states, including the Stokes-Adams syndrome.

Homografting of organs has, with one or two exceptions, only been successfully accomplished in identical twins.[22] Surgeons have the incentive to explore this field, and it may be that they will be able eventually to control the phenomenon of rejection by the host, so that hearts and lungs may be successfully homografted. We now have mechanical hearts and lungs capable of performing the cardiac and pulmonary functions outside the body. Will we be ingenious and clever enough to develop such artificial structures for use within the body? Indeed, one member of this Association has been so bold as to predict that artificial hearts within the thorax will be an actuality in 2 to 5 years.

We are just beginning to explore the effects of cold on cells, tissues, and organs. Much remains to be learned about rapid cooling and warming of the whole body and the biochemical effects of different rates of cooling and warming of the organs of the body. Hibernation is still a mystery. The solution of this mystery may have vast implications in the field of surgery. The preservation of the cellular elements of the blood without disruption of cellular structure by ice crystals, by controlling of the speed of cooling and the use of glycerol, is only a start. Much remains to be learned about the effects of temporarily slowing down metabolism by lowering the temperature. This knowledge is needed for the successful preservation of organs and tissues preparatory to homografting. It is an exciting age to live in, and I wish I were young again!

How shall this transition of thoracic surgery from youth to manhood be accomplished? What is needed to solve the problems which lie before us? Money is required to support investigators and technicians and to buy equipment and supplies. Laboratory space is needed in which to work. The money is here in abundance. The Department of Health, Education and Welfare

spent 44 million dollars in 1953 for medical research and 176 million dollars in 1958,[10] a fourfold increase in 5 years. There are hundreds of well-equipped surgical laboratories in this country and Canada and in many other parts of the world. These, however, are merely tools. The essential requirement is the investigator himself who must use these tools to dig knowledge from the morass of ignorance around us.

Many young men are studying today some of the problems which I have mentioned as well as many others. Have they been properly educated in the methods of scientific investigation? Are they being lent a guiding hand when needed by someone experienced in these methods? Have they been properly chosen to undertake these tasks? Are they engaged in research because of a genuine desire and excitement in solving a problem and contributing to man's knowledge? Or is the work an unimaginative chore to be gotten through with as quickly as possible and the results rushed into print, in order to further their advancement in academic rank in medical school and their professional reputation? Without impugning the integrity of the many devoted investigators working in our surgical laboratories, I fear the answer to the latter question is all too frequently in the affirmative. This is an unhealthy situation which results in the publication of many mediocre or worthless articles which should never see the light of day. Many good young surgeons interested in teaching and practice, I am sure, feel frustrated and baffled by this constant pressure to engage in research and to publish. As the Prophet said of the teacher, "If he is indeed wise, he does not bid you enter the house of his wisdom, but rather leads you to the threshold of your own mind."[15]

It is true that the good investigator is frequently an excellent teacher, but this is not invariably so. It is also true that an excellent teacher may have never engaged in research. Certainly the great medical schools of our country should have a place on their faculties for those who teach and investigate, and for those who teach but do no research.

Now let us consider the qualities of the man who is most likely to provide the solutions to some of the riddles confronting us. First of all, he need not be Neitzche's Superman,[23] but he must be honest with himself and others. As Polonius said, ". . . above all, to thine own self be true, and it must follow, as the night the day, Thou canst not then be false to any man."[24] The investigator must have a deep-seated integrity. His passion must be the discovery of the truth. He must be critical of any slipshod work on his part. He should not be anxious to report premature results, but should wait until his work is finished and has been well controlled. His desire should be to be right, and to produce the evidence that will convince others that he is right. The seeker after truth, therefore, must be the incorruptible man. If he be otherwise, he will not find the truth, but only illusory shadows of the real world which will mislead others as well as himself.

Second, this incorruptible man must have great patience, persistence, and industry. He must be willing to devote infinite attention to detail. He must cultivate preciseness. He will often be discouraged. What true investigator has not been? Picture Johann Kepler, working for 22 years, seeking to discover

the laws of planetary motion from Tycho Brahe's precise observations of the positions of the planets. Had Kepler been easily discouraged, he would never have formulated those majestic laws of motion of the planets around the sun.

Men with the qualities I have mentioned may never engage in research because they have no desire to do so. Frequently a brilliant medical student who graduates at the top of his class and has the aforementioned qualities may be put under pressure by the faculty of his medical school to engage in research. This is understandable, but undesirable. If a man does not want to do research, he will never be an investigator. The best way for a man to discover whether he is interested in research is for him to spend a period of time, seldom less than a year, working under supervision in a laboratory. During this trial period, he will discover whether research appeals to him or not; his supervisor will also quickly learn whether the beginner is a "self-starter." The man with potentialities as an investigator will see problems that need solution and will outline methods of approaching these problems. The methods he proposes may be inadequate because of his inexperience, but the fact that he recognizes the incompleteness of his knowledge in a certain area, and that he formulates an attack upon the problem, indicates that he is a potential investigator. On the other hand, the individual who spends the year intelligently and faithfully carrying out the suggestions of his supervisor, adding little or nothing of his own to the solution of the problem under consideration, is not the man to continue to do research.

I would thus suggest that in every institution where surgeons are educated and research facilities exist, the opportunity be presented to the embryo surgeon of spending a year in a laboratory if he so desires. Both he and his mentor will have a good idea at the end of that period as to whether he has a capacity for research. If he has not, the time will not have been misspent, because the year's experience will enable him to be a more critical reader of surgical literature during the rest of his professional life. On the other hand, he may experience a genuine excitement in discovery and great satisfaction in devising experiments which will indicate the truth or falsehood of his concept. This man is the true investigator. He must be encouraged and supported because he is the one who will add to the store of human knowledge.

Having discovered the man, how can we best further his progress? It is my belief that having completed his formal surgical education, he should then spend some time under the tutelage, guidance, and discipline of an experienced investigator. I believe that this second period is best spent at an institution other than the "parent" one, and that the investigator under whom he works should be engaged in research in one of the sister disciplines of medicine rather than in surgery. Both suggestions are made for the purpose of giving the young investigator greater perspective. This second period of research should prove to be an invaluable experience. The young investigator will learn something of the scientific method, how to use the necessary tools, the necessity for control experiments, and something about the errors in his methods and in his results.

In planning this second period in research, the young surgeon should select the investigator rather than the subject. He will learn from the man rather than from the subject under investigation. This, of course, is true of all educational experience. Any subject can be fascinating when illuminated by the mind of an inspiring teacher and investigator. I realize that others would point out the desirability of sending young surgeons who are potential investigators to other institutions to learn the techniques, tools, and methods of some basic science which might prove fruitful in its application to surgery. Nevertheless, the heart of the matter is the philosophy, the approach, the conduct of the experiment, and the handling of the results. This is the very essence of science and the scientific method. If the technology in a special field is essential to the solution of a problem, it can and will be learned easily. To put the technology before the philosophy of the scientific method is to put the cart before the horse.

Now as to the actual conduct of the research, perhaps the easiest way to approach the subject is to point out some common errors which may be made by the inexperienced. I shall discuss six of these. One is the failure to be aware of pertinent work by others in the field of investigation. The second is the failure to make a detailed plan of the conduct of the experiment or the failure to adhere to such a plan, when and if made. The third is the failure to evaluate continually the work in progress by calculating and studying, day by day, the results of the experiments performed. Fourth is the failure to perform adequate control experiments and to appreciate the errors in the techniques employed. Fifth is the failure to report *all* results no matter how bizarre they may appear. The sixth error is the drawing of unwarranted conclusions from the evidence.

The first error—not knowing the work of others in the field—is the least of the errors. Confirming the work of others, or repeating the work independently by a slightly different method, has value in itself. However, failing to give credit to the work of others in reporting one's own results is an egregious error and can be the source of great embarrassment, no matter how innocent the omission. This mistake is not likely to occur often because reading and studying the results of others in the field of inquiry should not only precede the research but should continue during the conduct of the experiments and, by the time the work is finished, the investigator should be well conversant with the results of others.

The second error—the failure to make a detailed plan—is not uncommon among the inexperienced. The youthful and enthusiastic investigator may perform a series of experiments, modifying each succeeding one in order to improve it, hoping like Mr. Micawber[11] that something better will turn up. After much hard work has been expended in this fashion, the investigator ends up with a series of observations, each one differing slightly from the one before, and with results, therefore, from which no valid conclusions can be drawn. One should make a careful distinction between such haphazard work and the performance of pilot experiments designed to help the investigator to arrive at a detailed plan, to which he must thereafter adhere. Such pilot work may prove to be a great saving in effort, time, and money.

The third error—failure to calculate and study the experimental results while the work is progressing—is a common fault in the unsophisticated investigator. In making the original detailed plan, some variable may have been overlooked which may vitiate the experimental results. Continued careful analysis of the results of the experiments in progress will reveal such an overlooked factor and obviate the performance of experiments without value. When such an overlooked factor is surely discovered, the plan of the experiment must then be altered. This continuous current analysis of results is always carried out by the sophisticated investigator to ensure that he remains on the path of exploration which he originally intended to follow.

The fourth error—the failure to perform control experiments—is perhaps uncommon. However, the control experiments performed may be inadequate or of insufficient variety. The investigator must be sure that the results he is reporting are due to the conditions which he has set up and not to some extraneous factor. Some control experiments may be performed before beginning the investigation, others concurrently with the investigation, and still others when the research has been completed. Those performed at the start are generally done to determine the errors inherent in the techniques to be employed. For example, duplicate determinations of cardiac output on normal individuals would certainly be performed before studying cardiac output in patients with pathologic conditions. The control experiments performed during the course of the investigation, and those performed at its conclusion, arise from an analysis of the experimental results and a realization that additional controls are necessary to rule out certain variables which may have influenced the results obtained.

The fifth error—failure to include all observations in reporting results—arises from human frailty. Our postulated, incorruptible man would be incapable of making this error, yet I suspect that it occurs more commonly than is realized. Suppose a series of experiments are performed with uniform and consistent results which tend to support the hypothesis which the investigator originally made and then, one day, the results of an experiment turn out to be grossly at variance with all the previous results. Regardless of how the researcher racks his brain to explain this sport, he is unable to see how the experimental procedure varied one iota from all the preceding experiments. What is more natural to the unsophisticated than to conclude that the experiment must have been performed under conditions differing from the others, although he is unable to say how it differed? Hence, the erroneous conclusion is reached that the results of this particular experiment should be discarded. To the sophisticated investigator, on the other hand, such a sport is welcomed and reported. A too consistent nicety of results disturbs him and an occasional sport is reassuring. There has been more than one instance in which a technical assistant has arranged matters so that the results which the investigator desires are consistently achieved beyond his fondest hopes. In my own laboratory, a number of years ago, we discovered that a technician was arranging the experimental results in this fashion.

The sixth error—drawing unwarranted conclusions from the evidence—is common in clinical reports in the surgical literature and is not uncommon in the reporting of research results. In the first place, the evidence may be insufficient to justify the conclusions drawn. For example, numbers in a series less than 100 have been expressed in terms of per cent sometimes carried to the first, or even to the second decimal point. This, of course, is absurd. The concept of significant numbers should be thoroughly comprehended by the young investigator. If a measurement can be justifiably expressed in only three significant numbers, then the results of calculations from these measurements cannot be expressed in four or five significant numbers. The figures would then indicate a degree of accuracy greater than was possible in the original measurements. This seems so obvious from the common sense point of view that it hardly needs stating, yet the surgical literature abounds with examples in which this is done.

Another mistake in reporting results is to apply elaborate statistical methods to figures which are quantitatively and qualitatively insufficient to justify such treatment. Inspection and common sense will frequently provide the clue as to what conclusions are justified and what are not. Finally, if results are reported accurately and completely, a good summary at the end of the article will frequently serve to round out the report, allowing the reader to draw his own conclusions from the evidence.

The following summary of my remarks is a good example of drawing conclusions from inadequate evidence or, indeed, from no evidence at all except the writer's experience and convictions. We have passed through a period in which thoracic surgery has shown an amazingly rapid growth. Much still remains to be done to increase the safety of the operations we perform, to learn more about the diseases we treat, and to devise methods and techniques for the therapy of diseases and congenital abnormalities which are now beyond the scope of our surgical capabilities. We have finances and laboratories but we need properly qualified and motivated men to find solutions for the problems which confront us. I believe that the subtle, or sometimes obvious, pressure on young surgeons today to engage in research should be done away with. The stimulation of the association with an experienced investigator should be all the incentive needed to arouse curiosity and interest in the younger members of our profession. Society will be better served by the concentrated endeavors of a few properly motivated and qualified investigators, adequately supported, than by the unenthusiastic and disinterested work of the many. I am confident that the future generation of surgical investigators will contribute to human knowledge in general, and thoracic surgery in particular, far more than those of us who are finishing our "work in the vineyards of surgery."[6]

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HONORED GUEST'S ADDRESS

THORACIC SURGERY IN THE COMMONWEALTH OF MEDICINE

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I AM immensely honored by the invitation to address this Association which has a greater influence on thoracic surgery than any guild, college, or Board. This estimate of your importance depends largely on reading with immense profit the papers and discussions of the Association as published in the JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, and noting so many of your names as distinguished contributors. May I remind you that your first President was Dr. Meltzer, whose mantle today has fallen on John Gibbon? The least historically minded know that the scientific endeavors of these two men have largely broken down two great barriers to surgical endeavor; the first encouraged us to explore the pleural cavity, the second the inner chambers of the heart. Meltzer and Auer[1] in 1909 were not being quizzically paradoxical when they entitled their famous paper "Continuous Respiration Without Respiratory Movements." Our President[2, 3] of today, courageously surviving years of, at times, disheartening toil, came to a triumphant day when, in this city, the right atrium was opened for the first time for the successful closure of a septal defect with the patient supported by extracorporeal circulation. Scarcely a generation ago we only dreamt of an effective circulation without adequate cardiac contractions, although in 1937 the President had published a paper pointing the way to such an achievement.

Reflecting on achievements as fabulous as these, the general medical observer would find it difficult to assign thoracic surgery to its correct place in the general corpus of medical science or to assess what such successes, with their investigational and technical implications, have contributed to the fuller comprehension of the biologic responses and behavior of man in health and disease. Admittedly the general biologist today may take over the study of many aspects of hypothermia, for its implications exceed those of cardiac or neurological surgery. Nonetheless, it would be difficult to deny that the rapidity with which cardiac surgeons seized on the opportunities provided by the hypothermic depression of metabolic and bodily functions intensified research into

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the whole subject. In this audience today are many surgeons (it would be a fulsome and lengthy task to catalogue the names, but I am happy and honored to share the company of so many great pioneers) who have not only laid foundations of primary biologic research on which thoracic surgery has grown, but have built massively and imaginatively on the original work of other scientists in many fields while making their own contributions in the wards, operating rooms, and laboratories. I believe that most of you would resent the suggestion that men interested in thoracic surgery have been responsible for that fragmentation of surgery which we deplore, when thinking in our armchairs by the fireside, but which at times in the hospital we appear to encourage when we become involved in specialized techniques that occupy many of our working hours and those of our associates working in general and cardiological medicine, radiology, hematology, and medical biochemistry.

Already you will have realized that I am shirking the presentation of a piece of original work and am treading the easier pathways of historical and educational reflections. Thoracic surgery is itself a hybrid flower, nourished by many different soils and agents, but scattering, as it grows older, seeds that, fertilized by other disciplines, have flourished in contiguous arid pastures to bear good fruit. These seeds, I believe, have an important part to play in the general field of medical education and biologic research. May I first be allowed to indicate that thoracic surgery has escaped at least one era of dangerous isolation, but that the recent startling developments of cardiovascular surgery have enabled many physiologic and technical procedures, originally confined to the surgery of the thorax, to be applied to the treatment of many other areas of the body. This should protect us in the future from sterile isolation.

THE DANGERS OF ISOLATION

The establishment of new surgical techniques, both investigational and therapeutic, has always depended on a certain bold aggressiveness which for a time may have offended the tenets of traditional classicism that may maintain false practices; this in the past has led to many unnecessary bloody noses. As a young general surgeon starting as a pupil of Morriston Davies and Price Thomas in 1934, the era of the lean, hard years of thoracic surgery, I was conscious of much opposition to the employment, before the wonderful discoveries of Fleming and Waxman, of surgery in the treatment of certain phases of pyogenic and tuberculous infections. Even at that time, notable books on thoracic surgery had been written by Sauerbruch,[4] Lilienthal,[5] Alexander,[6] and Morriston Davies[7]; but thoracic surgeons were working largely in isolation. Drainage of pleural and lung abscesses and collapse procedures for tuberculosis could be performed without intratracheal anesthesia; but once lobectomy requiring this type of anesthesia, performed for bronchiectasis and then for cancer, became established, a potential bifurcation of surgeons into extra- or intrapleural operators became possible.

Fortunately with the advent of surgical treatment of persistent ductus arteriosus, the correction of coarcted aorta, and operative attacks on the problem

of congenital cyanotic heart disease, thoracic surgery could no longer concern itself largely with infection* and neoplasm of the lung, but enlarged its territory to include a vast amount of truly physiologic and corrective surgery. This expansion dispelled forever the danger of surgeons working in the thorax in areas of narrow specialization. This renaissance of thoracic surgery, continuing in the two decades after 1938 and, including open cardiac work, developed so rapidly that many physicians working in other branches perhaps overlooked the significance of the new developments. The astonishing changes that took place, under the stimulus of men like De Bakey, in the surgery of the obliterative vascular disease of the great vessels, including the concept of segmental areas of disease and the ensuing clinical patterns of ischemia, have led to the extension of so-called thoracic expertise to extrathoracic organs, such as the brain or the kidney, and to a great amount of investigational work, much of it presented to this Association.

CONTRIBUTION OF THORACIC SURGERY TO MEDICAL EDUCATION

I believe that men working on thoracic surgical problems during these exciting years escaped confinement within towers of isolation because, as Blades[8] said in his Presidential address to this Association in 1958, "It would be difficult for surgeons who have fulfilled the qualifications for certifications in thoracic surgery to lose interest in general surgery." Today, University Departments of Surgery on the other hand would languish if they deprived their residents of thoracic surgical experience. The need for precision can be demonstrated well by examples from neurosurgery and thoracic surgery.

This slide demonstrates the help given to surgeons from a brief glimpse of cardiac catheter studies during actual surgical studies. This type of information is in increasing use in other fields of surgery during complicated surgical procedures.

In the two decades, before mitral valvotomy became an established procedure, surgeons working within the chest quite unconsciously acquired a respect from their medical colleagues because of their efforts to achieve precision in diagnosis and treatment; the thoracic surgeon quickly realized that he had no affection for lists of differential diagnoses. The rapid development in diagnostic radiology, endoscopy, exfoliative cytology, and the earnest encouragement of studies of respiratory function and of the hemodynamics of the central area of the two circulations were pointers to the dominant need for exact preoperative measurements. I believe that many of you at this period were the pathfinders to an era of astonishing revelation in the fields of respiratory, circulatory, and alimentary physiology. The collaboration of the medical men increased as surgical progress provided visual evidence to refute or confirm the assumptions of intellectual reasoning.

*The military surgeon during the last World War early realized that physiologic relief provided by decortication of the strangled lung in certain instances of hemothorax was followed by an astonishingly rapid clinical improvement.

The surgical attack on stenosed cardiac valves and congenital heart disease fortunately coincided with the increasing use of cardiac catheterization pioneered by men such as Cournand and MacMichael, leading to a combination of precision in the preoperative, operative, and postoperative phases in this early stage of cardiac surgery. This combination galvanized cardiology in general. This flow of new knowledge, followed by angiocardiography and left heart catheter studies, starting as a trickle has become a torrent which has opened into a wide lake since open cardiac work became established. Even before the value of this progress made in collaboration with medical men became obvious, great advances, especially in the study of pulmonary hypertension, due to many causes were made, and full explanations appeared for those distressing deaths from right ventricular failure that used to accompany lung resections for cancer in the pre-war days. The rapid application of this knowledge to the study of congenital heart disease had, and continues to have, a great educational as well as practical and research value, and is enabling an excellent program of physiologic and pharmacologic research to be practiced.

The systemic effects of many thoracic diseases are too obvious to require enumeration, for no one can deny the value of studying important diseases affecting respiration, circulation, and alimentation. Thoracic surgery provides excellent teaching material because of the rapidity of the changes that can be seen and measured accurately as they cause wide fluctuations in hemodynamics and the chemistry of the blood, and so on. But lest we forget that the study of clinical phenomena, as yet unexplained, is still a fruitful field of research, may I speak shortly on two problems—one connected with cancer of the lung and one with an esophageal disorder?

Everyone in this audience will from time to time have encountered bizarre systemic effects accompanying about 3 per cent of the patients with lung cancer who consult him. The phenomena I shall shortly list may accompany any type of lung cancer and, indeed occasionally, innocent tumors, such as a fibroma, located within the lung parenchyma. It may be that in the production of certain significant features remote from the chest that adenocarcinoma may be the commoner cause of the gross features of pulmonary osteoarthropathy as indicated by Flavell[9, 10] in 1953; in my own experience, however, these peculiar phenomena can often be associated with the rounded tumor which is so often a squamous carcinoma, not infrequently without lung symptoms. Perhaps in 30 to 40 per cent of patients with lung cancer, as well as in other intrathoracic conditions, such as lung abscesses and bronchiectasis, and in other states, such as congenital heart disease and cirrhosis of the liver, pulmonary osteoarthropathy is present. What I wish to draw particular attention to is that other extrathoracic symptoms and signs in addition to the osteoarthropathy may accompany lung tumors. Listing the bizarre conditions: (1) pulmonary osteoarthropathy, (2) rheumatoid arthritis, (3) peripheral neuritis, (carcinomatous neuropathy which may be motor or sensory or a combination of both), (4) cerebellar degeneration, (5) excessive, uncomfortable warmth of the limbs,

(6) gynecomastia, (7) a Cushing type of syndrome, and (8) myasthenia gravis. All these changes in the type of patients I refer to occur without detectable evidence of metastases in systems other than the thorax. Flavell referred particularly to the florid type of pulmonary osteoarthropathy and to the neuropathy. Russell Brain,[11] speaking in Philadelphia in 1958, described in considerable detail the neurological syndromes which may be associated with carcinoma in the absence of malignant cells in neural tissue. Such a neuropathy as he described undoubtedly occurs with cancers situated other than in the lung but, of his 43 patients, 32 had bronchial tumors. Neither he nor Flavell included instances of patients with gynecomastia, the Cushing type syndrome, and myasthenia gravis, although undoubtedly they know of these conditions. The important point known by many thoracic surgeons is that, after resection of the tumor, regression of all of these symptoms, with disappearance of the physical signs commonly follows, and that the clinical improvements commence within a few hours of surgical ablation. One exception to this predictable amelioration is in patients with cerebellar changes; postmortem examination shows that irreversible degeneration of the neural cells is the rule. Many contributions to the literature dealing with clubbed fingers, arthritis, and peripheral neuritis have been made, and it would be inappropriate in an address of this type to attempt to summarize them.

I have had several patients in whom the neuropathy has been associated with osteoarthropathy, gynecomastia, and uncomfortable, "hot" limbs. This latter feature is capable of exact scientific measurement; investigation by plethysmography usually discloses an increase of the lower limb blood flow from 4 to 8 times the normal. On the day after operation, if the tumor has been resected, the plethysmographic data indicate an immediate return of the blood flow to normal levels, with instant disappearance of the feeling of uncomfortable warmth. I have 7 patients in this category. In 2 patients presenting at the hospital with gynecomastia as the only symptom (both were over 50), radiographs of the chest in the absence of symptoms disclosed a circular tumor. After removal of the tumor, the gynecomastia disappeared rapidly. In addition, I have seen 3 patients presenting with Cushing type syndromes, obvious because of the swelling of the face and the other manifestations accompanying that condition. Two of these patients returned to normal appearance within a week of resection of the pulmonary tumor. In addition, I have seen 2 patients presenting with all the classical features of myasthenia gravis who were found to have pulmonary, not thymic, tumors.

Flavell, in describing the relief of joint symptoms which followed division of the vagus on the side of the chest harboring an inoperable cancer, noted that this procedure relieved the symptoms as rapidly as the ablation of the tumor itself, and referred to Hansen's observation, 1952, that removal of the neural plexus around the pulmonary hilum gave a similar result. Wyburn Mason[13] in 1948 noted similar relief in a patient after ligation of the pulmonary artery in the course of an operation in which excision of the lung was being undertaken but proved to be impossible because of the nature of the tumor's extensions.

At the same time, thoracotomy alone in inoperable cancer associated with these types of symptoms fails to provide any relief, and this in itself is some indication that the immediate change is not due to steroid response associated with the stress reaction which accompanies major surgery.

THE ETIOLOGY

I will not weary you with the many theories or hypotheses that have been put up to explain this type of syndrome; a great deal of work has been done on investigation of clubbing of the fingers and osteoarthropathy. The rapid relief which follows the three procedures just mentioned seems to indicate that removal of a septic focus is not acceptable as indicating infection as the main etiological factor. That a humoral influence or influences is at work seems clear, and also that this is in some measure under the control of neural influence affecting the lung. We are at once in a wide field of speculation; that the steroids play a part is indicated by the rare example of gynecomastia and the "hot feet" syndrome and at once brings to mind a possible connection with a substance, such as serotonin. We are investigating this problem in several departments, and we are indeed right in the middle of the Commonwealth of Medicine. I note that in this program Dr. Bernatz, Dr. Clagett, and Dr. E. G. Harrison are considering the problem of thymic tumors and find a disturbance in the serum proteins and alterations in the adrenal cortical function. We are attempting investigations in the problem along these lines but the results are confusing and I do not dare to attempt an interim report. We are investigating, in addition to proteins and steroids, the possible influence of 5-hydroxytryptamine. The moment the surgeon involves himself in that fascinating substance he rapidly realizes the great gaps in physiologic and hematologic knowledge; I mention this fascinating problem to support my theme that more than ever we live in a community of medical scientists all anxious to help each other and with each attempt to explore such problems we at least gain further evidence of our ignorance.

I am indeed delighted that your Association does not allow questions to its guest, for I should soon be lost in a morass of unjustified speculations.

AN ESOPHAGEAL PROBLEM

Before I finish, may I detain you for a few minutes with this slide? This is a roentgenogram of a barium swallow made of a man of 31 years of age who, for 10 years, had suffered from severe heartburn and 3 months before this picture was taken developed considerable dysphagia. On esophagoscopy the stricture you can see was shown to be high up in the esophagus and was readily passed with an esophagoscope. A biopsy of the esophagus above this stricture revealed normal esophageal lining. Immediately below the stricture, biopsy fragments showed gastric and small intestinal structure. Three centimeters above the estimated position of the esophageal hiatus, what looked like a functional cardia was seen; no esophageal tissue was found in biopsies from the

stricture to this point. At operation, carried out by my colleague, L. D. Abrams, a small hiatal hernia was present. The peritoneal reflections from the abdominal cavity reached up above the hiatus for 3 cm. The "esophagus" itself had no peritoneal covering above this layer. The hernia was easily repaired and, although "gastric" tissue exists above this level, the dysphagia has disappeared and the patient swallows normally with no heartburn. Presumably this is a "gastric lined esophagus" (for such my friend Philip Allison would, I think, call it, while my other friend Normal Barratt might designate it as the lower esophagus lined by columnar epithelium).

If I may be allowed to speculate, the rapid relief of symptoms is due to the fact that the hiatal hernia repair has prevented the upward escape of irritant gastric juice, whereas the "gastric" tissue within the esophagus itself lacks the vicious qualities of the peptic ulcer producing juice.

My excuse for mentioning this type of problem is that frequently I find patients with esophageal strictures ascribed by different authors to many different causes, but which usually in my experience have somewhere lurking in the background evidence of the evil effect of reflux esophagitis. I skate over this difficult problem once more knowing that I shall not be subjected to probing questions: The precise knowledge preoperatively of the anatomy and pathology of this type of gullet prevents the performance of unnecessarily mutilating operations.

CONCLUSION

I must not exceed the prerogative of the guest who outwears his welcome by staying and speaking too long on the doorstep of departure. I think all of you in this audience would agree with me that we are fortunate people to have been allowed to work on the problems of thoracic surgery in a most exciting epoch and that we are indeed fortunate to be paid for doing what we enjoy doing. I do not think you are an arrogant selection of men and I believe you have made great contributions to the general Commonwealth of Medicine, being at the same time only too ready to thank many in other fields of medical science for their help and encouragement. When I read the proceedings of this Association I often have the feeling that its deliberations are not studied sufficiently by men working in other fields. At times I think we too may have short periods of isolation when we are slightly tainted by applying to ourselves the brush of minor arrogance and ignorance. To remind myself of my own deficiencies I have in mind some lines written by a failed medical student who became a great, and I think neglected, poet. I refer to Francis Thompson[14] when he wrote:

> Science, old noser in its prideful straw,
> That with anatomizing scalpel tents,
> It's three inches of the skin and brags
> All's bare.

Surgeons who daily look into the inner recesses of what was long regarded as the ultimate barrier know that all is not bare. They will continue in their

quests until the full mystery of the contraction of the individual cardiac muscle fiber has been revealed. If the members of this Association continue, as I know they will, along the lines just indicated by the President, a surgeon may indeed be the one to clarify that biologic wonder.

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ISOLATED STENOSIS OF THE PULMONIC VALVE ASSOCIATED WITH PULMONARY TUBERCULOSIS

A Report of Two Patients Treated Surgically

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IN 1843 Craigie[5] first reported a case of pulmonary tuberculosis associated with isolated congenital stenosis of the pulmonic valve. Since then, numerous reports have stated that tuberculosis is more frequent and more serious in patients with pulmonic stenosis.[1, 8, 11, 17]

A retrospective analysis of roentgenograms and clinical data of 800 patients submitted to operation for pulmonic stenosis, predominantly cyanotic, in Blalock's clinic between 1944 and 1950 led Sloan, Hanlon, and Scott[16] to the conclusion that the incidence of tuberculosis in this admittedly rather young group was less than 2 per cent, which they considered "not excessively high." In Soulié's clinic,[17] the incidence of pulmonary tuberculosis was 5.1 per cent in 196 patients with pulmonic stenosis, isolated or combined, which was significantly greater than the incidence of 1.2 per cent in 250 patients with congenital heart disease without pulmonic stenosis. Mattson[11] reported the incidence of post-primary pulmonary tuberculosis—irrespective of activity—in patients who underwent cardiac catheterization between 1948 and 1956 in Stockholm. Evidence for tuberculosis was found in 16.3 per cent of 49 patients with pulmonic stenosis, pure or in combination, but in only 0.7 per cent of 148 patients with congenital heart disease without pulmonic stenosis.

Thus, although control groups have been generally limited, the evidence points to a rather high incidence of pulmonary tuberculosis in patients with pulmonic stenosis.

The recent encounter of 2 adult patients with symptomatic severe isolated pulmonic stenosis and active pulmonary tuberculosis prompted the present report.

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CASE REPORTS

CASE 1.—R. B. (B.C.H. No. 1540603), a 52-year-old male cook, entered the hospital in April, 1955, with weakness and shortness of breath.

In 1951 he had entered the Boston City Hospital for the first time with weakness, sweats, fever, palpatation, dyspnea, and chest pain. A systolic heart murmur had been discovered 5 years earlier. Examination revealed enlargement of the heart and a thrill and a systolic murmur in the pulmonic area. The blood pressure was 106/80 mm. Hg. He had right ventricular hypertrophy demonstrated by electrocardiogram. Roentgenograms of the chest showed enlargement of the right ventricle and dilatation of the pulmonary artery, and angiocardiograms showed marked delay in emptying of the right ventricle. Blood cultures were negative. Because of persistent fever and a palpable spleen, a full course of penicillin and streptomycin was given.

In June, 1953, the patient was readmitted with progressive dyspnea, orthopnea, palpitations, and ankle edema. He was in advanced congestive heart failure with an irregular heartbeat at 130 per minute, blood pressure of 104/90 mm. Hg, distended, pulsating neck veins, hepatomegaly, and pitting edema to the knees. The heart spontaneously reverted to normal sinus rhythm and subsequently responded well to digitalis and diuretics. A cardiac catheterization was performed. The right ventricular systolic pressure was 104 mm. Hg. The brachial arterial systolic pressure was 102 mm. Hg. The pulmonary artery was not entered.

On readmission in April, 1955, because of dyspnea, weakness, sweats, palpitation, and cough, the patient appeared chronically ill. The blood pressure was 155/110 mm. Hg. A prominent *A* wave was seen in the neck. There was marked cardiac enlargement with a left parasternal heave and a diffuse apical impulse. The first pulmonic sound was loud and snapping, the second pulmonic sound decreased, and there was a loud third heart sound. A rough Grade 4 systolic murmur was heard diffusely over the precordium, loudest in the pulmonic area. There was dullness and decrease of vocal and tactile fremitus over the right apex anteriorly, where breath sounds were decreased and bronchial. Inspiratory râles were heard anteriorly and posteriorly over the right apex. The liver was enlarged. The electrocardiogram showed sino-auricular tachycardia at 110 with incomplete atrioventricular block, broad notched P waves, and right bundle branch block. The R wave measured 9 mm. in Lead V_1. The tracing was indicative of right ventricular hypertrophy and strain. Fluoroscopy and roentgenograms of the chest indicated enlargement of the right ventricle and pulmonary artery. There was moderately advanced cavitary tuberculosis in the right upper lobe (Fig. 1, *A*). The sputum was positive.

Cardiac catheterization on April 14, 1955, showed a mean right atrial pressure of 8 mm. Hg with a prominent *A* wave. Right ventricular pressure was 200 systolic, 0 diastolic, and 10 mm. Hg end-diastolic. Simultaneous brachial arterial pressure was 73/55, 62 mean. The pulmonary arterial pressure was 23/15, 17 mean. The pulmonary wedge pressure was 4 mm. Hg. Fluoroscopy and records of pressure during withdrawal of the catheter suggested that this severe pulmonic stenosis was valvular. Blood oxygen contents did not differ significantly in right-sided chambers. The arterial oxygen saturation was 92.7 per cent, but rose to 100 per cent on breathing oxygen.

The patient was transferred to the sanatorium division and treated with streptomycin, 1 Gm. twice weekly, and para-aminosalicylic acid, 12 Gm. daily. In November, 1955, the latter was stopped because of gastrointestinal symptoms, and isoniazid, 300 mg. daily, was started. The sputum remained intermittently positive, and there was only slight improvement in the tuberculous lesion (Fig. 1, *B*).

On Nov. 29, 1955, transarterial pulmonary valvotomy was performed. The approach was through a left third interspace incision. A Dacron cuff was sewn to the lateral surface of the enlarged pulmonary artery. The valve was a rigid cone with a 3 to 4 mm. opening in the apex. The largest Brock valvulotome (diameter 1.4 cm.) was then passed through the valve via the cuff down into the right ventricle. The new opening in the valve was checked

with the finger and found to be only 8 mm. in diameter. Even after vigorous digital dilatation, the opening measured no more than 1 to 1.2 cm. A special curved pair of scissors with blunt tips was used to cut the valve to the ring, using digital guidance. The scissors were rotated 180 degrees and a second cut was made to the ring. The finger could then be passed into the right ventricle practically to the apex with ease. No appreciable infundibular narrowing was found in systole. It was estimated that the valve opening in systole was at least 2 cm. in diameter. The previously felt jet stream was now much softer and diffuse,

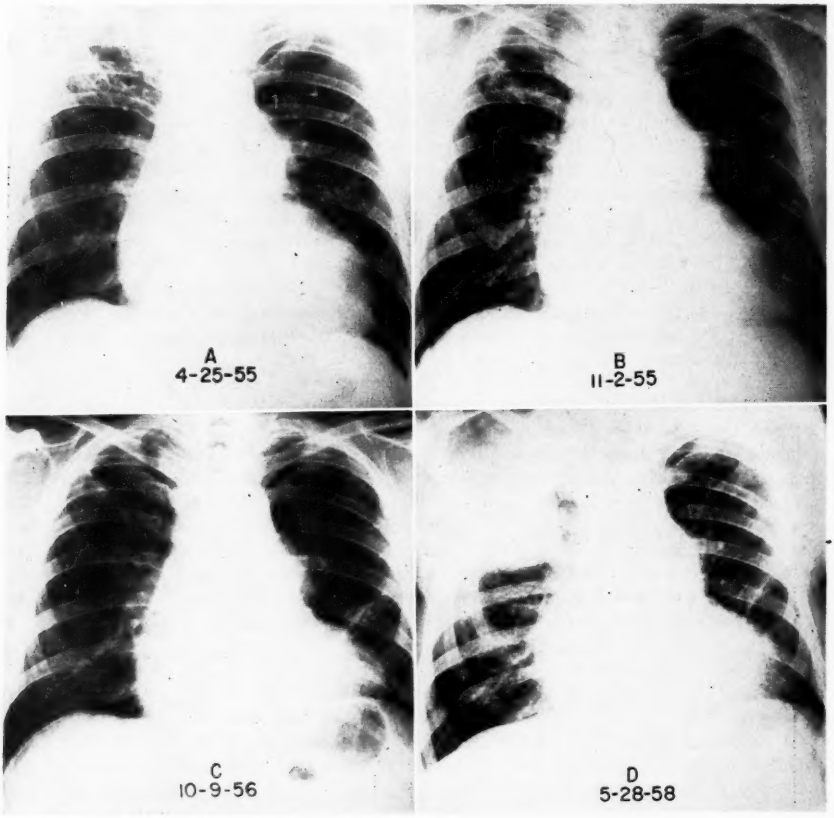

Fig. 1.—Chest roentgenograms of Case 1, R. B.

A, April, 1955: Moderately advanced tuberculosis with cavitation in the right upper lobe, before treatment.

B, November, 1955: Only slight improvement in the lesion after 6 months' therapy.

C, October, 1956: Eleven months after pulmonic valvotomy. Marked regression of infiltration. Laminograms showed persistent cavity at the right apex.

D, May, 1958: One and one-half years after right plombage thoracoplasty, followed by conversion.

and the right ventricle contracted more completely. The systolic pressure gradient across the pulmonic valve had decreased from 120 to 12 mm. Hg during the operation. During partial closure of the pericardium, the patient developed ventricular tachycardia at 240 beats per minute. After 1.5 Gm. of procaine amide administered intravenously, the rate slowed to 150 and normal sinus rhythm at 100 beats per minute became re-established The patient's post-

operative course was benign, and he was returned to the sanatorium for additional rest and chemotherapy.

On Dec. 21, 1955, a postoperative cardiac catheterization revealed a right atrial mean pressure of 5 mm. Hg. The *A* wave was still prominent. The right ventricular pressure was 25 systolic, 0 diastolic, 5 end-diastolic. The pulmonary arterial pressure was 18/7, 9 mean. Pulmonary wedge pressure was 5 mm. Hg. The brachial arterial pressure was 130/90, 102 mean. The cardiac index was 2.7 L. per minute per square meter. Again, there was no evidence of associated defect.

The patient became asymptomatic and did well clinically. Sputa were negative after March, 1956. In October, 1956, chest films (Fig. 1, *C*) showed regression of the infiltrative lesion, but laminograms showed persistent cavitation in the right apex. Bronchoscopy, including bacteriologic studies, was negative.

On Nov. 20, 1956, a plombage thoracoplasty on the right was performed. The clinical course continued benign, and sputa and gastric aspirations remained negative. The patient was discharged in May, 1957, and was to continue taking streptomycin and isoniazid.

In the summer of 1957 he was fully ambulatory and worked as a part-time painter. Streptomycin was stopped, but he continued to take isoniazid 300 mg. daily and resumed para-aminosalicylic acid, 12 Gm. daily, until May, 1958 (Fig. 1, *D*).

He has remained essentially asymptomatic, compensated and stable. In December, 1958, 3 years after pulmonic valvotomy, the blood pressure was 160/110 mm. Hg. The second pulmonic sound was of normal intensity. There was a Grade 2 pulmonic systolic murmur The liver was just palpable. The electrocardiogram showed sinus arrhythmia at 80, incomplete atrioventricular block, and right bundle branch block. The R wave in Lead V_1 measured 4 mm. Comparison with preoperative tracings showed marked improvement in S-T segments and T waves and reduction in right ventricular strain.

Subsequently, he resumed full-time work as a chef and has remained clinically well and asymptomatic.*

Comment: This 52-year-old man with severe isolated valvular pulmonary stenosis survived presumptive bacterial endocarditis at age 48, developed congestive heart failure at age 50, and subsequently manifested cavitary pulmonary tuberculosis and also labile systemic hypertension. The tuberculous lesion did not respond well to rest, streptomycin, and para-aminosalicylic acid. Pulmonic valvotomy 7 months after initiation of therapy was effective and successful, both clinically and physiologically. After 3 months sputa were negative. The patient was fully rehabilitated. More than 4 years later, he remains asymptomatic with a compensated circulatory system and a healed tuberculous lesion.

From a technical point of view, this case illustrates one of the reasons for failure of some "closed" pulmonary valvotomies. The initial partial incision and dilatation of the valve were inadequate and increased the diameter from 4 mm. to only 8 mm. Incision of the valve to the ring under digital guidance was completely effective.

CASE 2.—J. J. (B.C.H. No. 1623869), a 23-year-old housewife and factory worker, was admitted in October, 1956, because of a menstrual disorder. A heart murmur had been discovered during scarlet fever at the age of 8. She had had an uneventful pregnancy at age 16. An electrocardiogram taken 1 year later showed right ventricular hypertrophy. She remained asymptomatic except for slight dyspnea on running up three flights of stairs in her early twenties.

Examination revealed a well-developed, apparently healthy, young Negro woman. There was a right ventricular heave. The second sound was faint at both aortic and pul-

*The authors are indebted to Dr. Isadore Starr of Laconia, N. H., for a follow-up report dated Feb. 8, 1960.

monic areas. There was a harsh Grade 4 pulmonic systolic murmur, well transmitted over the precordium and into the neck. The blood pressure was 120/80 mm. Hg. The lungs were clear. The electrocardiogram showed sinus arrhythmia at 50 and right ventricular hypertrophy with R wave 14 mm. in height in Lead V_1. Flouroscopy and roentgenograms of the chest showed slight cardiac enlargement with definite right ventricular enlargement and moderate dilatation of the main pulmonary artery. The lung fields were clear. A clinical diagnosis of isolated pulmonic valvular stenosis was made.

On Oct. 18, 1956, cardiac catheterization was carried out. Although the catheter repeatedly entered the right ventricular ouflow tract to the level of the pulmonic valve, the pulmonary artery could not be entered. Right atrial mean pressure was 5 mm. Hg, with a prominent A wave. The right ventricular systolic pressure was 130 mm. Hg, the brachial arterial systolic pressure was 134 mm. Hg. The right-sided cardiac chambers showed no significant difference in oxygen content. The arterial saturation was 93.6 per cent. The findings were compatible with the clinical diagnosis. Operation was advised but refused by the essentially asymptomatic patient.

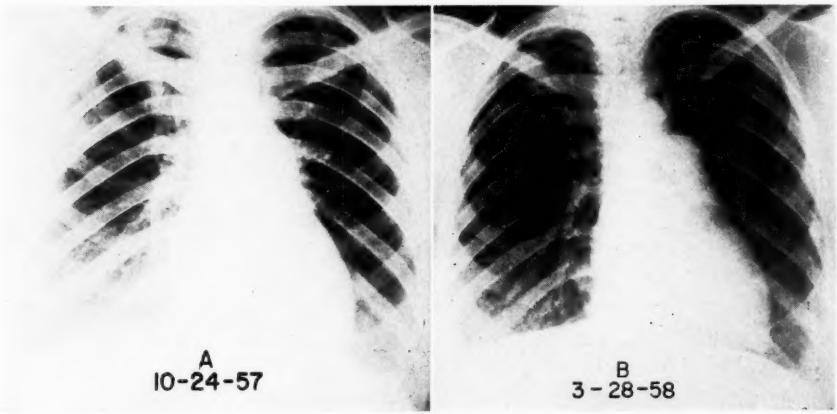

Fig. 2.—Chest roentgenograms of Case 2, J. J.
A, October, 1957: Moderately advanced, infiltrative tuberculosis of the right upper lobe.
B, March, 1958: Excellent response after 5 months' treatment.

She was readmitted in October, 1957, with a history of mild exertional dyspnea of 6 months' duration, occasional precordial pain, palpitation, dizziness, and intermittent swelling of the feet after standing. For 3 weeks prior to admission she had also noticed increasing nonproductive cough and fatigability. The cardiovascular examination was unchanged. On auscultation of the chest, post-tussive râles were heard over the right upper lobe posteriorly. Chest x-ray films revealed infiltrative, moderately advanced, pulmonary tuberculosis of the right upper lobe (Fig. 2, *A*). The sputum and gastric aspirates were positive for *Mycobacterium tuberculosis* on smear and culture. The electrocardiogram showed right ventricular hypertrophy and strain. Catheterization of the right side of the heart was repeated on Nov. 5, 1957. Again, the catheter entered the right ventricular outflow tract freely, but did not enter the pulmonary artery. Right atrial mean pressure was 4 mm. Hg, with a high A wave. The right ventricular pressure was 136 mm. Hg systolic, 7 end-diastolic, and the brachial arterial pressure was 116 systolic, 16 diastolic, and 80 mean. Right heart chambers showed no significant difference in oxygen content and the arterial oxygen saturation was 96.8 per cent. The cardiac index was 3.2 L. per minute per square meter.

The patient was transferred to a sanatorium and treated with bed rest and para-aminosalicylic acid, 12 Gm daily, and isoniazid, 600 mg. daily, for 6 months. The sputum and

gastric aspirates became negative in December, 1957, and the lesion in the right upper lobe receded and almost disappeared (Fig. 2, *B*).

On April 20, 1958, she was readmitted, and on April 22 a transventricular pulmonary valvotomy (Brock procedure) was done. The valve was explored through the ventricle with a 4 mm. probe. A Brock fish-tailed valvulotome, 1 cm. in diameter, was guided through the valve opening. A Brock aortic valve dilator was then introduced and the valve engaged and dilated slowly but forcibly to full extent of the dilator (3.5 cm). A definite tearing sensation was felt and the open dilator could be passed into the pulmonary artery with ease from the ventricle. The previously felt sharp jet became much more coarse and diffuse, and the right ventricle contracted much more completely.

The patient's postoperative course was uneventful and she was discharged on maintenance doses of para-aminosalicylic acid and isoniazid. By June, 1958, she had returned to full activity as a housewife, without symptoms, with negative sputum and gastric aspirations. Chest x-ray studies showed only a small linear scar in the right upper lobe. Cardiac examination revealed a slight right ventricular heave. The pulmonic ejection click had disappeared and the second pulmonic sound had increased in intensity. The pulmonic systolic murmur was less loud, but still Grade 3. The electrocardiogram showed normal sinus rhythm at 88, decrease in right ventricular strain, and reduction of the R wave in V_1 to 9 mm.

On July 7, 1958, cardiac catheterization was repeated. The pulmonary artery was now entered with ease. Right atrial mean pressure was 6 mm. Hg, right ventricular pressure 30 systolic, 6 end-diastolic, and pulmonary arterial pressure was 19 systolic, 6 diastolic, and 11 mean. The mean systolic pressure gradient across the pulmonic valve was 10 mm. Hg, at a cardiac index of 3.1 L. per minute per square meter.*

Comment: This asymptomatic 23-year-old housewife with severe isolated valvular pulmonic stenosis refused operation. Six months later she developed cardiac symptoms and after another 6 months had moderately advanced pulmonary tuberculosis.

The tuberculous lesion responded very well to rest, para-aminosalicylic acid and isoniazid. After another 6 months, a transventricular pulmonary valvotomy was performed. The stenosis was effectively corrected by means of a dilator with an expanding head, which opens wider than most conventional pulmonary valve dilators.

Incidence of Tuberculosis in Patients With Pulmonic Stenosis at the Boston City Hospital.—An analysis of the population from which the above 2 cases have been drawn was considered pertinent. Only individuals aged 12 or older have been included.

During the 4 years, 1955 through 1958, 15 patients with pulmonic stenosis, ranging from 14 to 50 years in age, underwent cardiac catheterization at the Thorndike Memorial Laboratory. Of these, stenosis was isolated in 13 and associated with other defects in 2. It was severe in 9 and mild in 4. The 2 patients just reported were the only ones with tuberculosis. Thus the incidence of active tuberculosis was 13.3 per cent over-all, 18.2 per cent for the group with severe stenosis and 22.2 per cent for the group with isolated severe stenosis. Mattson[11] reported an incidence of 16.3 per cent in 49 patients with proved pulmonic stenosis.

During the same period, 1955 through 1958, 212 patients with heart disease without pulmonic stenosis were catheterized in this laboratory. (This group

*In October, 1960, J. J. delivered a healthy infant after a normal pregnancy.

included 149 patients with rheumatic heart disease, in most of whom some degree of pulmonary hypertension was present.) Only 1 of these had or is known to have developed active pulmonary tuberculosis. This was a 37-year-old man (B.C.H. No. 1563731) with active cavitary tuberculosis, fibrosis and emphysema, and cor pulmonale.

A review of the files of the Mallory Institute of Pathology at the Boston City Hospital disclosed that during the 60 years from 1897 through 1956, 10 cases of pulmonic stenosis had been entered, of which 4 were isolated and 6 were associated with other congenital defects. Tuberculosis was present in 1 case of isolated pulmonic stenosis and in 1 case of pulmonic stenosis associated with a ventricular septal defect.

DISCUSSION

The most interesting aspect of the presumptive increased susceptibility of patients with pulmonic stenosis to pulmonary tuberculosis is the implication for the pathogenesis of the tuberculous lesion. Soulié and his group[17] observed a greater incidence of tuberculosis in congenital lesions with decreased pulmonary blood flow than in congenital heart disease with increased pulmonary blood flow (vide supra) and concluded that the former favored the development of pulmonary tuberculosis. When Mattson[11] analyzed 413 patients with congenital heart disease or mitral stenosis according to the level of pulmonary arterial pressure, he found that pulmonary tuberculosis was present in 1 per cent of 261 patients with pulmonary hypertension, but in 13 per cent of 61 patients with pulmonary hypotension. Review of Soulié's 17 cases in which cardiac diagnosis was proved[17] reveals that 13 patients had pulmonic stenosis in association with a presumptive right-to-left shunt, 3 had congenital heart disease without pulmonic stenosis but with left-to-right shunts, and 1 had tricuspid atresia and developed pulmonary tuberculosis 5 years after surgical production of a left-to-right shunt. This sample, then, did not include any cases of isolated pulmonic stenosis with tuberculosis. Mattson's 9 proved cases of congenital heart disease and pulmonary tuberculosis included 6 cases of pulmonic stenosis associated with presumptive right-to-left shunt, 2 cases of isolated pulmonic stenosis, and 1 case of presumptive left-to-right shunt.[11]

We must ask the question, What do the above cases of congenital heart disease and tuberculosis have in common? Evidently the answer is not "decreased pulmonary blood flow," or "decreased pulmonary arterial pressure," which applied only to some. Furthermore, if the bronchial circulation is included in our consideration, the evidence for increased bronchial collateral blood flow to the lung in pulmonary atresia and tetralogy of Fallot[3, 9] raises serious question as to whether it is appropriate to consider the tetralogy of Fallot as associated with decreased pulmonary blood flow. The incidence of tuberculosis has been found increased when either pulmonary arterial pressure was low or when pulmonary arterial blood was arterialized, and the highest incidence has been described under conditions associated with both of these factors. Conversely, high pulmonary arterial pressure associated with decreased saturation of pulmonary

arterial blood for oxygen, such as is found in patients with mitral stenosis or chronic left ventricular failure, has been considered to protect from pulmonary tuberculosis,[11, 13, 19] even though characterized by low pulmonary blood flow. Indeed we have never seen a patient with severe mitral stenosis and active tuberculosis.

In summary, then, the clinical experience suggests that pulmonary arterial blood at a low hydraulic pressure but with a high partial pressure of oxygen and low partial pressure of carbon dioxide favors the tuberculous process, while pulmonary arterial blood at a high pressure but with low partial pressure of oxygen and elevated partial pressure of carbon dioxide does not create an environment favorable for the tuberculous lesion.

This hypothesis finds some support in experimental studies. The growth of *Myco. tuberculosis* is favored by high tension of oxygen[4, 12] and inhibited by high partial pressure of carbon dioxide.[6, 7] In 1950, Hanlon, Scott, and Olson[10] reported that surgical anastomosis between systemic and pulmonary arteries in monkeys with intravenously induced tuberculosis resulted in extensive caseous tuberculosis in the lung on the side of the anastomosis. Similar extensive lesions were seen after ligation of one pulmonary artery, lateralizing to that side.[14]

These experimental data led to the expectation that shunt operations for the treatment of the tetralogy of Fallot might be followed by activation of latent pulmonary tuberculosis. However, there is no evidence that this has taken place.[16, 20] One difference between the experimental monkeys and patients with tetralogy of Fallot and operative left-to-right shunt should be pointed out: the arterial oxygen tension in the patients is abnormally low.

Therapeutic Considerations.—If pulmonic stenosis favors the development of pulmonary tuberculosis, might it not also interfere with normal response to therapy? This possibility was considered when treatment was being planned for the 2 patients presented. The following treatment plan was formulated: Initial sanatorium care with stress on bed rest (increase in perfusion pressure and pulmonary blood flow to the upper lobes) combined with chemotherapy. If the tuberculous lesion were to show slow or no response to therapy within a few months, pulmonary valvotomy was to be carried out, as in the first case. If, on the other hand, the tuberculous process showed response to treatment, arrest of the lesion was considered desirable before proceeding to cardiac surgery, as in the second case.

Others have attempted surgical treatment of this combination of lesions, namely, pulmonic stenosis and pulmonary tuberculosis.

It is of historical interest that the first report of successful pulmonic valvotomy by Sellors[15] concerned a patient with tetralogy of Fallot and advanced bilateral pulmonary tuberculosis.

Sloan, Hanlon, and Scott[16] in 1954 reported their attempts to resect tuberculous lesions in a patient with pulmonary atresia, who had undergone a Blalock operation on the uninvolved side 3 years earlier, and in a patient with

tetralogy of Fallot, in whom a Blalock operation had been performed at the same time. Both patients died on the day of operation of hemorrhage from collateral blood vessels to the lung.

In 1955, Soutter, Scannell, and Myers[18] reported the case of a patient with severe valvular pulmonic stenosis, associated with an atrial septal defect, diabetes mellitus, and persistently active bilateral pulmonary tuberculosis, who was treated successfully by combined transarterial valvotomy and left pneumonectomy, although considerable right ventricular hypertension remained postoperatively. Björk and Bagger[2] in 1958 reported 2 patients with pulmonic stenosis who were treated with simultaneous pulmonary valvotomy and resection of lung for tuberculosis. The first patient had isolated infundibular and possibly also valvular stenosis, which was at most partially corrected by the initial combined operation and later necessitated further infundibular resection. The second patient had severe valvular pulmonic stenosis and a slight right-to-left shunt at the atrial level. The transarterial pulmonary valvotomy was effective, but the combined operation was followed by an infected hemothorax and bronchopleural fistula.

Against this background of reported cases with treatment for pulmonic stenosis and active pulmonary tuberculosis, the management of the patients reported here stands out as remarkably successful and effective. The tuberculous lesion of the patient with pulmonic stenosis thus may show excellent response to present-day treatment. Also, the "closed" approach to the pulmonic valve has been demonstrated to permit effective correction of valvular pulmonic stenosis.

Our experience and that of others recorded in the literature does not justify rules of treatment for patients with pulmonic stenosis and active tuberculosis. We are willing to say, however, that when cardiac compensation can be maintained under conditions of rest therapy, a course of conservative antituberculous treatment should be administered. If the nature of the lesion or the response of the patient is such that surgical treatment of the tuberculous disease is indicated, this is best preceded or accompanied by pulmonic valvotomy.

The hazard of pulmonary tuberculosis should be added to the complication of subacute bacterial endocarditis and the risk of congestive heart failure in evaluating the medical prognosis of the patient with severe pulmonic stenosis, a lesion treatable surgically.

SUMMARY

Two adult patients with severe isolated valvular pulmonic stenosis and active pulmonary tuberculosis, both in heart failure and disabled, are reported in detail.

Both patients were initially treated with bed rest and chemotherapy. Pulmonic valvotomy was performed subsequently and was clinically and physiologically effective as demonstrated by postoperative cardiac catheterization and clinical course. The tuberculous lesion healed prior to cardiac surgery in the 23-year-old woman. In the 52-year-old man, the sputum did not become nega-

tive until after pulmonic valvotomy, and persistent cavitation was treated by plombage thoracoplasty. Both patients have been fully rehabilitated.

Therapeutic principles are discussed in the light of the probable pathophysiology underlying the tendency of these two diseases to co-exist.

We are grateful to Dr. G. Kenneth Mallory for his permission to review the files of the Mallory Institute of Pathology.

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EXFOLIATIVE CYTOLOGY IN SOLITARY PERIPHERAL LESIONS OF THE LUNGS

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PERIPHERAL round lesions are the most common variety of early carcinoma of the lung. While there is a rich literature concerning the nature, diagnosis, and treatment of these lesions, little has been written about the importance of exfoliative cytology as a diagnostic procedure.

The purpose of this paper is to review 53 cases of circumscribed peripheral lung lesions seen at the University of Maryland Hospital and to correlate the cytologic studies with the clinical picture presented, the bronchoscopic findings, and the histopathologic diagnosis.

MATERIALS AND METHODS

It is apparent that the reliability of cytologic examination is dependent on the quality of material received. The following methods are suggested and partially followed in the cases surveyed.

1. *Sputum Collection.*—Upon awakening, the patient coughs deeply and directly in a wide-mouth container which is brought immediately to the laboratory for processing. Areas containing tissue particles or blood-streaked elements are removed under direct good lighting conditions and smeared on ten prepared slides, then fixed immediately in 95 per cent alcohol. The six best smears are stained with a modified Papanicolaou stain, three of them are screened routinely, but in case of a suspicious smear all six or ten smears are examined.

2. *Direct Collection of Bronchial Secretion.*—Bronchial secretions at bronchoscopy are treated as ordinary sputum. The bronchus is washed with normal saline and then aspirated. The washings are sent immediately to the laboratory, centrifuged, and ten smears made, any remaining material is imbedded and sectioned.

The interpretation of the smears is reported as follows: (1) Positive–when there is no doubt of malignancy. (2) Inconclusive–when abnormal but not definitely diagnostic cells are present. Repeats are requested. (3) Negative–

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when normal elements are seen only. (4) Unsatisfactory–when too scanty, or with no carbon-bearing histiocytes or with too much inflammation masking the diagnostic cells.

A complete cytologic study of the bronchial secretions of a patient should at least include the examination of five consecutive morning sputa and one or several bronchial washings. Antibiotics, bronchodilators, and detergents are routinely used to prevent bronchial blockage and promote drainage by reducing mucosal congestion.

REVIEW OF THE LITERATURE

In reviewing the literature, the cytology of solitary lesions was found only in papers dealing with bronchogenic carcinoma as a whole. Farber[2] in his review of 241 bronchogenic carcinomas found 60 peripheral lesions, 36, or 60 per cent, had positive cytologic findings. Jennings and Shaw[5] reported 42 peripheral tumors with 27 cases (64.3 per cent) of positive sputa. Hood and associates[4] studied 156 cases of solitary circumscribed lesions of which 15 patients who had bronchogenic carcinoma had cytologic studies with 8 (53 per cent) positive results. Spjut and co-workers[6] had 11 (40 per cent) positive cytologic examinations reported out of a total of 27 cases of peripheral solitary pulmonary lesions; of 124 cases of coin lesions reported by Ford and Kent,[3] 59 were proved malignant but 23.75 per cent of the patients only had tumor cells in the sputa. Vance and his group[7] reported positive cytologic findings in 20 of 64 cases (31 per cent) of peripheral lung lesions. Wilkins[8] had only 3 positive cases cytologically of a total of 32 known bronchogenic carcinomas and one of them turned out to be a false positive. Davis and Peabody[1] and Wolpaw[9] believed that exfoliative cytology was of little value in the diagnosis of a bronchogenic carcinoma presenting as a solitary nodule.

PRESENTATION OF DATA

To be included in this series, the lesion had to be peripheral, round, and circumscribed. Those lesions displaying cavitation or distal bronchial obstruction were excluded. Fifty-three cases satisfied these criteria and constitute the present study. Thirty-two of these lesions were malignant and 15 were benign. The age distribution in the malignant group was 48 to 78 years and 23 to 67 years in the benign. There were 5 females in the malignant group and 4 in the benign group, a sex ratio of 6.4:1 and 4:1, respectively. Fig. 1 shows the distribution of the lesions in the various lobes of the lung.

Symptoms.—Circumscribed solitary lesions are often thought of as asymptomatic and are detected usually on routine radiography of the chest. In the present series, 11 patients (21 per cent) only were asymptomatic while the remaining 41 complained of one or combination of chest pain, cough, or hemoptysis. Cough was the commonest symptom, it occurred in 62 per cent of the patients with malignant lesions and 65 per cent with benign lesions. Chest pain was next in frequency, it was found in 32 per cent of patients with malignant lesions and 50 per cent in benign cases. Hemoptysis, thought

to be the most important significant symptom of a malignancy (Hood and associates[4]), was more common in our series in benign lesions (50 per cent), than in the malignant ones (22 per cent). The correlation of the symptoms with the cytologic findings will be discussed later in the paper.

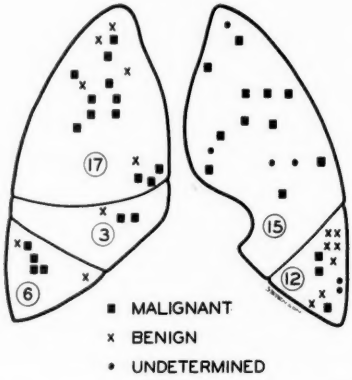

Fig. 1.—Graph illustrating the distribution of the benign and malignant lesions.

RESULTS

Table I outlines the wide range of diagnosis encountered in this study. All the proved cases were diagnosed by operation or at autopsy, the patients with probable carcinomas had no histologic diagnosis but had rib or brain metastasis.

TABLE I. PATHOLOGIC CLASSIFICATIONS

	Cases	
Malignant Neoplasms		
Squamous cell carcinoma	20	
Adenocarcinoma	4	
Metastatic carcinoma	3	
Probable bronchogenic carcinoma with metastasis	5	
Total		32
Benign Lesions		
Tuberculoma	7	
Actinomycosis	1	
Coccidioidomycosis	1	
Bronchogenic cyst	1	
Inflammatory	3	
Spur of thoracic vertebra	1	
Aneurysm of thoracic aorta	1	
Total		15
Undetermined	6	
Total		53

Correlation of the cytologic diagnosis with the final pathologic diagnosis was as follows: There were positive cytologic findings in 12 cases, all of which were proved or probable carcinomas, except in 1 patient who was not

operated upon. Five cases were proved to be squamous cell carcinoma, 1 adenocarcinoma, 2 metastatic carcinomas, and 3 probable bronchogenic carcinoma. There were no false positive results in this series. Fifteen cases were reported as inconclusive: 9 proved to be squamous cell carcinoma, 2 adenocarcinoma, and 1 metastatic carcinoma. Only 2 cases in which there was inconclusive cytologic diagnosis proved to be benign; 1 was inflammatory and the other lesion was an actinomycotic granuloma.

There were 9 cases of carcinoma which were missed by cytology; 6 patients had squamous cell carcinoma, 1 adenocarcinoma, and 2 had no histologic diagnosis but had rib metastasis. Failure of detection in these cases was due to (1) non-involvement of the bronchial mucosa by the lesion and (2) insufficiency of the material submitted for examination.

We tried to correlate our cytologic findings with the material examined, the clinical symptoms, and the size of the lesion in order to determine whether these factors affect the detection rate of malignant solitary lesions.

When a complete sputum series was examined, 11 out of 12 malignancies were detected. When bronchial washings and less than 3 sputa were examined, 4 were detected and 3 were missed. When bronchial washings were examined alone without any sputum, 9 were detected and 5 were missed. This proves the importance of examining a complete sputum series before ruling out the presence of cancer.

When the symptoms are correlated with the cytologic diagnosis, hemoptysis was present in 6 and cough in 16 of the detected cases, whereas these symptoms occurred in only 1 and 6 of the nondetected group. Although the series is small, yet it is apparent that patients presenting with cough and hemoptysis have a better chance of having their lesions detected cytologically than asymptomatic patients; the reason being that hemoptysis is probably due to involvement of the bronchial mucosa by tumor. Most of the malignant cells were found in the smear taken from the blood-streaked zones of the sputum examined.

Bronchial involvement was seen directly by bronchoscopy in 7 patients with lesions near the hilum. Six of them had positive bronchial biopsy.

According to Spjut and co-workers, a definite correlation exists between the size of the lesion and the cytologic diagnosis. The average size of the malignant lesions which were detected in this series was 4.8 cm. compared to an average of 5 cm. of the malignant lesions which were not detected. However, a breakdown of the cases into their various sizes, as shown in Table II, confirms the observation that a larger number of cases was detected among the larger lesions.

TABLE II. RELATION OF SIZE OF SOLITARY MALIGNANT LESION TO DETECTION RATE*

SIZE	DETECTED LESIONS	NOT DETECTED
2-3 cm.	7	4
3-4 cm.	2	1
>4 cm.	13	4
Total	22	9

*Size of lesion not available in 1 case.

DISCUSSION

Solitary lung lesions have long been a source of controversy, both from a diagnostic and therapeutic point of view. The diagnosis cannot be established in the majority of cases except by thoracotomy. Bronchoscopy is not often helpful unless the lesion is near the hilum where it can be visualized and biopsied. In this series of 32 cases, bronchial visualization and biopsy of the lesion was possible in 6 cases only. On this basis we agree with Hood and his colleagues[4] that exfoliative cytology seems to be the most useful laboratory means available for the establishment of a positive preoperative diagnosis in patients with circumscribed lesions of the lung. The interesting features of this study are the absence of any false positive results and the confirmation of the validity of the inconclusive ones in 87 per cent of the cases. Besides, it shows the advantage of a complete sputum series in cytologic work. The difficulty of interpretation of the abnormal cells seen is mainly due to the general poor differentiation of the peripheral malignant neoplasms of the lung and the degeneration seen in most of the exfoliated cells, since they have a longer distance to cover before being expectorated.

The false negative smears were reviewed in retrospect to determine whether malignant cells could be identified; only in 1 case was this possible. This demonstrates the adequacy of the screening procedure and proves that the failures may be ascribed to the absence of malignant cells in the sputum and bronchial washings, to the inadequacy of the material submitted, to the non-involvement of the bronchial mucosa by the neoplasm, or to the presence of a proximal bronchial obstruction.

SUMMARY

Exfoliative cytology was studied in 53 cases of solitary circumscribed lesions of the lung. Cytologic examination was positive in 11 cases and inconclusive in 12 cases out of 32 malignant lesions. Failure of detection was due either to the peripheral location of the tumor with lack of bronchial involvement or inadequacy of the material submitted for examination. There were no false positive results and all the inconclusive reports proved to be malignant except in 2 cases. A complete sputum series is essential for the proper detection of malignant lesions among the solitary lung nodules.

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EXPERIENCES IN THE MANAGEMENT OF RECURRENT SPONTANEOUS PNEUMOTHORAX

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THE TERM "pneumothorax" was first used in the year 1803 by Itard to define the accumulation of air in the pleural cavity. However, the disease entity itself had been described in the year 1767 by Hewson.[1, 2, 4] In the 100-year period from 1803 to 1903, more than 350 articles appeared in the medical literature on various phases of the problem.[4] The physical findings in pneumothorax were recorded in 1819 by Laennec[2] and thus the clinical diagnosis of the condition was enhanced.

From time to time the causes of spontaneous pneumothorax have come under the scrutiny of the medical profession. Until the last three decades it had been assumed that tuberculosis was invariably the cause of the condition. For example: in 1880, from the analysis of a series of 986 cases of pneumothorax, Biach attributed the etiology to tuberculosis in 77.8 per cent. As late as 1931, Palmer and Aaft believed that 80 to 90 per cent of all cases of pneumothorax were caused by tuberculosis.[4] By contrast, however, as early as 1915 the role of the rupture of subpleural blebs in the development of spontaneous pneumothorax was described by Hayashi.[1] Today we recognize that the majority of pneumothoraces are secondary to rupture of emphysematous blebs or bullae.[5, 6]

Individual cases of spontaneous pneumothorax have been reported with diverse groups of diseases. For the most part, the entity may be attributed to relatively simple mechanisms, all of which afford a communication between the pleural space and functioning lung or patent bronchi. The communication may be direct or it may be devious but it nonetheless must exist to permit intrapleural air collection. The exceptions to this exist when air is introduced from a hollow viscus or from the outside, as in an open chest wound, or as a therapeutic measure in artificial pneumothorax or pneumoperitoneum. This, however, could hardly be described as spontaneous.

Without enumerating all possible causes, a few of the more common can be mentioned. Spontaneous pneumothorax may follow pulmonary infection, as in the rupture of a cavity or an abscess due to tuberculosis, coccidioidomycosis, staphylococcus, or other pathogens. Tumors, either primary or meta-

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static, may destroy the tissue barrier between intrapulmonary air and the pleural space. Further, pneumothorax may occur as a result of ball-valve obstruction of a bronchus. In this situation air is not allowed to leave a given area of lung and accumulates under pressure distal to the obstruction until there is alveolar rupture. The air may then dissect proximally along vascular sheaths to the hilus of the lung where penetration of the pleura occurs. Frequently in this situation the air may remain localized in the mediastinum.

In our experience the most frequent cause of spontaneous pneumothorax is pulmonary emphysema which may be either localized or diffuse. In this present series of patients with recurrent pneumothorax, we have been concerned almost exclusively with grossly localized emphysema as the underlying etiological condition (92 per cent of patients). The repeated rupture of localized or generalized emphysematous blebs and bullae is a serious problem, with attendant morbidity as well as economic loss in both the young and elderly. It has been our policy to strongly urge corrective surgery after a patient's second unilateral episode of spontaneous pneumothorax or after single bilateral pneumothoraces. Obviously in a military population such as ours the recurrent disability of repeated pneumothoraces is inconsistent with performance of any type of effective military duty. We have not been able to discover a case of recurrent pneumothorax due to tuberculosis.

MATERIAL

In the present study we have followed a total of 56 consecutive patients who have received surgical therapy for unilateral recurrent spontaneous pneumothorax. These people have been followed from 1 to 9 years, with an average follow-up of 4.1 years. Recurrent pneumothorax was caused by localized emphysematous blebs in 92 per cent of the patients. The others had a more diffuse type of emphysema except for 1 patient who harbored a bronchogenic cyst. Forty-nine of the group were treated by open thoracotomy, with bilateral staged procedures being done in three instances. Seven underwent closed tube thoracotomy with talc poudrage by insufflation.

The age range of these patients was from 18 to 40 years, with a mean age of 25.8 years. All but 3 were male soldiers and all but 1 were Caucasian—the one exception being an American Indian.

Included in this series are 7 individuals (12.6 per cent) who, in addition to recurrent unilateral pneumothorax, had a contralateral pneumothorax preoperatively. In two instances, bilateral pneumothoraces occurred simultaneously, a situation which is extremely rare. Of the cases of unilateral pneumothoraces, 53.2 per cent were right sided and 46.8 per cent were on the left.

The gross findings in 52 thoracotomies follow.

Pathologic Findings at Operation.—Localized emphysematous blebs in the apical and posterior position of the upper lobe, 45; diffuse lobar emphysema, 3; diffuse emphysema (all lobes), 1; bronchogenic cyst simulating giant emphysematous bleb, 1; and not specified, 2.

Operative Procedures.—Wedge resection of apical blebs and abrasion of pleura, 31; wedge resection of apical blebs and talc poudrage, 6; scarification or poudrage alone, 5; wedge resection alone, 3; segmental resection alone, 4; lobectomy, 2; and excision of bronchial cyst and decortication, 1.

As this report is primarily concerned with the problem of recurrent spontaneous pneumothorax, the prior treatment of previous episodes of pneumothorax is also included.

Prior Treatment of Pneumothoraces.—Bed rest until re-expansion, 30; thoracentesis (single and multiple), 8; and closed tube drainage, 18.

It is also noted that 2 patients treated with thoracentesis had had the introduction of sclerosing agents into the pleural cavity as part of their previous therapy. This consisted of 5 per cent silver nitrate solution in 1 case and a hypertonic glucose solution in the other case. Both solutions were unsuccessful in preventing recurrence of pneumothorax.

RESULTS

Forty-four of the total of 56 patients have been closely followed by questionnaires to the present time, with an average follow-up of 4.1 years. This constitutes 78 per cent of the original group. There has been but a single instance of postoperative recurrence of pneumothorax at the site of operation in this group of patients followed. This happened in a 40-year-old individual who was treated by talc poudrage alone after finding diffuse emphysema of the right upper lobe at open thoracotomy. Subsequently, a right upper lobectomy was performed. Three years have passed without further difficulty.

There have been no deaths in this series, and the complication rate has been 7 per cent. The most serious complication occurred in the only case of recurrence, cited above, and consisted of acute renal failure in the immediate postoperative period. This was treated by artificial kidney dialysis with recovery. The remaining complications consisted of persistent lung leaks requiring either repeated thoracenteses or re-intubation, and one minor incident of bleeding.

In addition to the 7 patients who demonstrated bilateral spontaneous pneumothoraces prior to definitive treatment, follow-up revealed that 9 other patients subsequently developed spontaneous pneumothorax on the contralateral side at varying intervals after the original operation without recurrence on the operated side. This was presumably on the basis of similar apical blebs as demonstrated on the side of thoracotomy in this group. Thus, a total of 16 (28 per cent) of the 56 patients developed a contralateral pneumothorax at one time or another.

DISCUSSION

It has been our policy to regard recurrent spontaneous pneumothorax as a problem warranting a definitive surgical attack on the underlying pathologic anatomy. After a second pneumothorax has occurred, operation has been

strongly urged. According to reports in the literature, the expectancy for recurrence following re-expansion of an initial pneumothorax is anywhere from 15 to 60 per cent.[4] The expected frequency of further recurrence is then proportionately higher. In addition, we have felt that the initial episode of spontaneous pneumothorax warrants more aggressive therapy than it customarily receives. Although a high percentage of pneumothoraces will absorb spontaneously, the re-expansion will be greatly hastened by active measures.[7] This may be accomplished by simple needle aspiration or, in the event that this is not successful, chest tube drainage of the pleural space with employment of suction may be indicated. If this latter procedure is properly performed and maintained, results will be uniformly successful. Thus the lung is re-expanded early and the leak usually firmly sealed. Undesirable residual air space and trapped lung are avoided. In addition, the patient is protected in the event of the serious complication of having a simultaneous spontaneous pneumothorax on the contralateral side. This occurred in 7 patients before surgery and in 9 others during the follow-up period; in a total of 56, this is indeed a serious consideration.

Re-expansion of the lung in cases of recurrent pneumothorax prior to operation has been generally accomplished by closed tube drainage. Thereafter, the patient is fully evaluated as to the advisability of a definitive surgical procedure. Chest roentgenograms do not always show the localized blebs that we have so consistently encountered at operation, but it is usually possible to distinguish these cases preoperatively from the diffuse emphysematous processes that are not amenable to resectional surgery. As mentioned previously, the most consistent finding has been localized blebs in the apical and posterior position of the upper lobe. These cases are considered ideal for the procedure of wedge resection of the blebs combined with abrasion of the pleural surfaces with dry gauze to the point of capillary bleeding. In this way the underlying pathologic condition is removed and recurrence is prevented by creation of a pleural symphysis. Where more extensive pulmonary disease is encountered as would require segmental resection or lobectomy for complete removal, this has been done without hesitation but not without reluctance. Here the possibility of prolonged lung leak and the need for subsequent tailoring thoracoplasty is considerably increased. Occasionally the process may be so extensive that only abrasion of the pleura may be carried out. If a large solitary cyst is found, resection is completed as simply as possible and followed by pleural abrasion.

For a time in 1956, talc poudrage of the pleural space was employed as a method of promoting adhesions in a small group of patients. However, it is our belief that wedge resection and scarification by abrasion is the superior method. Persistent pleural pain secondary to a talc granuloma has been noted in one instance and this has been one reason the procedure has been replaced, despite its apparent effectiveness in leading to pleural symphysis. Our only postoperative pneumothorax occurred in a patient with diffuse emphysema who had had an open talc dusting procedure.

Pleurectomy[8, 9] is not considered to be necessary solely for the purpose of inducing pleural adhesions. It is believed that this can be accomplished by a less extensive operation. Pleurectomy is usually attended by a small but definite danger of postoperative bleeding and, as such, complications and morbidity may be significantly increased.

SUMMARY

Fifty-six patients who had recurrent spontaneous pneumothorax are presented. Seven were treated with closed tube thoracotomy with talc poudrage by insufflation. The remaining 49 patients underwent a total of 52 open thoracotomies, 3 patients having bilateral stage procedures. The usual finding consisted of apical blebs (45 instances). The definitive treatment generally consisted of wedge resection of the blebs combined with pleural scarification.

Current follow-up in 78 per cent of the patients revealed a single isolated recurrence in a patient who was inadequately treated by present standards.

In addition to the management of recurrent spontaneous pneumothorax by aggressive surgical measures, it is our opinion that more active treatment of the initial episodes is warranted for medical as well as economic reasons.

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ARTERIAL OXYGEN, CARBON DIOXIDE, AND pH LEVELS IN PATIENTS UNDERGOING PULMONARY RESECTION

Intraoperative and Early Postoperative Observations

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TUBERCULOUS patients with limited ventilatory ability are subject to increased morbidity and mortality risks after thoracic surgical procedures.[1] Complications which may arise during and after operation in these "bad risk" patients include the development of respiratory acidosis from inadequate alveolar ventilation.[2, 3] It is also known that hypoxemia may occur and persist for variable periods of time after thoracic surgery.[4, 5] The relation of CO_2 retention and hypoxemia to such other complications as shock, ventricular fibrillation, and atelectasis has been discussed,[5-8] but their relationships to respiratory function, as preoperatively assessed, is not clear. Moreover, the nature and sequence of changes in respiratory blood gas levels have been studied with conflicting results.[8, 9]

This paper describes observations on respiratory gas exchange before, during, and after thoracic surgery in patients with varying degrees of ventilatory disability as judged by preoperative function testing. The findings are compared with those obtained from the usual ventilatory tests and lung volume measurements. The investigation included studies on (1) the effect of premedication, (2) the effectiveness of artificial ventilation during anesthesia, (3) blood gas values during spontaneous breathing in the early postoperative period, and (4) gas exchange in patients with early postoperative atelectasis or poor lung expansion.

Alveolar ventilation/blood flow relationships were also determined at rest and exercise before operation and at intervals during the first postoperative year; the results are the subject of a forthcoming report.[10]

MATERIAL

Sixteen patients were selected for study at the time of their preoperative case review. Eight of them (Group A) had clinical and spirometric evidence of moderate to marked ventilatory disability (restrictive or obstructive). The

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TABLE I. CLINICAL AND SPIROMETRIC DATA FOR PATIENTS UNDERGOING PULMONARY RESECTION—GROUP A WITH MODERATE TO SEVERE VENTILATORY FUNCTION, GROUP B WITH MINIMAL REDUCTION OF VENTILATORY FUNCTION

PATIENT AND AGE		DIAGNOSIS	PREOPERATIVE VC (% PRED.)	MVV* (% PRED.)	SPIROMETRY RV/TLC (%)	RESECTION AND EARLY POSTOPERATIVE COMPLICATIONS
Group A						
B. O.	49	Tuberculosis; RUL bronchiectasis and cavity; thick peel on rt.; emphysa	78	79	52	RUL decortication; atelectasis RLL
K. K.	50	Tuberculosis; bronchiectasis and cavity in LUL and superior segment LLL; emphysa	91	64	53	LUL and superior segment LLL and thoracoplasty; poor expansion LLL
O. W.	62	Destroyed left lung with cavitation (TBC); emphysa	75	63	40	Left lung with tracheoplasty
Osk. J.	58	Tuberculosis; bronchiectasis and cavity under rt. thoracoplasty	63	39	53	Apical and posterior segments of RUL
S. P.	54	Bronchogenic carcinoma in middle lobe	81	70	40	Right lung
L. G.	28	Tuberculosis; bronchiectasis in LUL and superior segment LLL; chronic extensive lesions rt. lung	59	26	39	LUL and superior segment LLL; thoracoplasty; poor expansion LLL
A. W.	56	Tuberculosis; bronchiectasis and cavity in LUL; cleared spread and closed cavity rt. lung	93	69	39	LUL and part of superior segment of LLL; poor expansion LLL
M. L.	37	Tuberculosis; main bronchial stenosis and destroyed left lung; cleared spread and closed cavity rt. lung	67	29	39	Left lung; prophylactic tracheostomy
Mean	49		76	55	45	Six bronchopulmonary segments
Group B						
T. L.	57	Tuberculosis; bronchostenosis with atelectasis of RUL; cavity in superior segment of RLL	88	64	36	RUL and superior segment RLL; RML atelectasis
C. G.	44	Tuberculosis; bronchiectasis and cavity in RUL	106	76	30	Right upper lobe; moderate air leakage
R. K.	59	Tuberculosis; bronchiectasis and cavity in LUL; fibrocalcinosis RUL	90	78	30	LUL and thoracoplasty; LLL poorly expanded
K. G.	17	Tuberculosis; caseonodose residual in RUL	103	77	25	RUL; poor expansion of RLL
R. N.	44	Tuberculosis; cavity left apex; cleared spread to LLL	110	83	26	Apicoposterior segment of LUL; atelectasis in parts of rt. and lt. LL's
H. S.	57	Nonspecific middle lobe bronchiectasis	119	94	27	Middle lobe; small atelectasis in RLL
M. M.	22	Tuberculosis; bronchiectasis and cavity RUL; cleared spread to RLL	84	92	20	RUL and thoracoplasty
Osb. J.	36	Nonspecific middle lobe atelectasis	99	85	26	Middle lobe; poor expansion RLL
Mean	42		100	81	28	Three bronchopulmonary segments

*Maximum voluntary ventilation or maximum breathing capacity.

diagnosis of obstructive emphysema was made in 3 of them. The resection performed averaged six bronchopulmonary segments. Eight others with minimal exertional dyspnea and much less evidence of ventilatory dysfunction were also followed for comparison (Group B); an average of three bronchopulmonary segments were resected in this group. Table I gives the clinical and spirometric data for all patients.

METHODS

Ventilatory tests and lung volume determinations (closed circuit helium) were performed using a Knipping spirometer and the results compared to the normal values of Lundgren[11] for men, and Baldwin and associates[12] for women. Terms and abbreviations are those recommended by Pappenheimer[13] and Gandevia and Hugh-Jones.[14]

Arterial blood was drawn using an indwelling polyethylene catheter in the brachial artery.[15] The blood was analyzed spectrophotometrically for oxygen saturation and capacity, using a method developed by one of us (S. S.-S.) and recently described by Holmgren and Pernow.[16] It was also analyzed potentiometrically for pH, using the Radiometer pH meter. The CO_2 tension was obtained by use of the above-mentioned pH value and the pH values obtained after equilibrating aliquots of the blood with gases of known CO_2 tensions. Bicarbonate levels were derived from the Van Slyke-Sendroy nomogram.

Specimens for blood gas analysis were drawn: (1) one or more days before operation; (2) after premedication, prior to induction of anesthesia; (3) during the operation after ligation of the pulmonary artery branches to the involved area; (4) at the end of the 1 to 3 minute period of relative apnea associated with suturing the open bronchial stump; (5) 5 to 10 minutes after extubation, after transfer of the patient to his bed but before he was taken from the operating room (the patient breathing room air spontaneously); (6) 1 to 2 hours postoperatively*; (7) 3 to 4 hours postoperatively*; (8) on the following morning, and (9) one week after surgery. In case of atelectasis or poor expansion of lung, arterial blood gases were analyzed more frequently.

Anesthetic management was characterized by:

(a) premedication with 10 to 15 mg. of morphine and 0.4 to 0.6 mg. of scopolamine or atropine, except for 5 patients (see Table II) who received 100 mg. of N(1-methyl-3-piperidylmethyl)-phenothiazine (Lacumin*)[17];

(b) induction with 250 to 500 mg. of enhexymal sodium (Evipan sodium†), respiration assisted with equal parts of nitrous oxide and oxygen, and 18 to 24 mg. of d-tubocurarine;

(c) orotracheal intubation followed by cuff inflation;

*During these periods oxygen was being administered by nasal catheter at flows of 2 to 4 L. per minute.

*Lundbeck & Co., Malmö, Sweden.

†Bayer, Leverkusen, Germany.

*Maximum voluntary ventilation or maximum breathing capacity.

(d) maintenance with nitrous oxide: oxygen in a 3.5:1.5 ratio, 50 to 250 mg. (average 150 mg.) of meperidine and, if necessary, repeated doses of 6 mg. curare;

(e) manually controlled ventilation in a semiclosed circuit with a respiratory rate of 20 to 25 per minute, an inspiratory pressure of 12 to 25 cm. of water, and a tidal volume of 300 to 500 ml.; an inspiratory: expiratory time phase ratio of 1:3 was used, allowing intrapulmonary pressure to fall to zero during expiration;

(f) during the period of suturing the open bronchial stump, administration of oxygen alone at approximately 5 L. per minute (this procedure was always preceded by a period of hyperventilation with the usual N_2O–O_2 mixture);

(g) spontaneous breathing with assistance after closure of the pleural cavity, tapering off the amount of nitrous oxide administered in oxygen so that the patients awoke within 5 minutes after the operation, still on the operating table.

The duration of the operation ranged from 1 hour, 45 minutes, to 6 hours, 45 minutes (average 4 hours, 5 minutes). The pleural cavity was drained and active suction of 10 to 30 cm. H_2O was maintained postoperatively. Immediately after the operation, before the patient was transported to the ward, a chest roentgenogram was obtained in the X-ray Department. During this period the pleural suction was discontinued.

Several of the patients in Group A (ventilatory dysfunction) were considered to fall into the "bad risk" category and *certain measures* were therefore taken. These included: (1) accentuation of the preoperative training and the postoperative insistence upon deep breathing and effective coughing (this work was carried out by physiotherapists and specially trained nurses), (2) close observation postoperatively for adequate ventilation and bronchial toilet with frequent nasotracheal suction when indicated, and (3) planned tracheostomy with a cuffed cannula and assisted ventilation in cases in which respiratory insufficiency was judged to be impending.

RESULTS

Mean values for the arterial blood studies during and up to a week after operation are shown for the two groups of patients in Fig. 1. Group A had preoperatively a lower oxygen saturation than Group B and a little increase of the bicarbonate level.

Slight changes occurred in arterial CO_2 tension levels in association with premedication and these changes are subdivided in Table II according to whether morphine-scopolamine or Lacumin were given. There was no significant effect of Lacumin on the CO_2 level in either of the two patient groups. Morphine-scopolamine on the other hand raised the CO_2 tension in both patient groups; the CO_2 tension reached pathologic levels only in the dysfunction group.

Both groups were kept low in arterial carbon dioxide (alevolar hyperventilation) and were well oxygenated intraoperatively, even after the period of ventilatory embarrassment associated with definitive suturing of the open bronchial stump. Immediately postoperatively, however, the patients of both groups retained carbon dioxide, Group A (dysfunction group) to the point

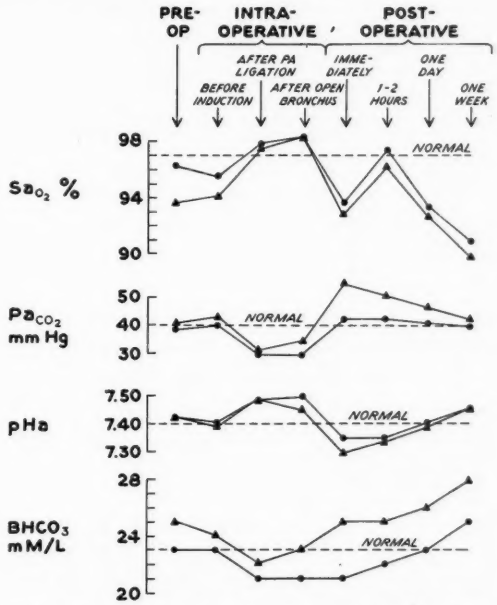

Fig. 1.—Arterial blood values before and up to 1 week after pulmonary resection—mean values for patients with ventilatory disability (Group A, *triangles*) and patients with minimal dysfunction (Group B, *circles*), including oxygen saturation (Sa_{O_2}), carbon dioxide tension (Pa_{CO_2}), pH, and bicarbonate ($BHCO_3$). High oxygen concentrations were breathed intraoperatively and in most of the patients at the time of sampling 1 to 2 hours after operation.

TABLE II. EFFECT OF PREMEDICATION ON ARTERIAL CARBON DIOXIDE TENSION, COMPARING MORPHINE-SCOPOLAMINE WITH PHENOTHIAZINE DERIVATIVE, LACUMIN

PATIENT	GROUP	PREMEDICATION	ARTERIAL CO_2 TENSION (MM. Hg)		CHANGE
			BEFORE PREMED.	AFTER PREMED.	
B. O.	A	Morphine-scopolamine	46	—	—
K. K.	A	Morphine-scopolamine	38	42	+4
O. W.	A	Morphine-scopolamine	45	49	+4
Osk. J.	A	Morphine-scopolamine	40	48	+8
A. P.	A	Morphine-scopolamine	39	46	+7
L. G.	A	Lacumin	42	43	+1
A. W.	A	Lacumin	42	41	−1
M. L.	A	Lacumin	37	35	−2
T. L.	B	Lacumin	43	42	−1
C. G.	B	Lacumin	39	41	+2
R. K.	B	Morphine-scopolamine	41	41	0
K. G.	B	Morphine-scopolamine	29	38	+9
R. N.	B	Morphine-scopolamine	40	40	0
H. S.	B	Morphine-scopolamine	32	32	0
M. M.	B	Morphine-scopolamine	42	41	−1
Osb. J.	B	Morphine-scopolamine	39	44	+5

of a significant acidosis (average pH 7.30 and tension 55 mm. Hg), and Group B (minimal dysfunction) had a pH of 7.35 and came up to only normal CO_2 tension (average 42 mm. Hg).* The arterial CO_2 tension immediately after operation correlated with the preoperative residual volume/total lung capacity ratio ($r = 0.63$) and vital capacity ($r = -0.63$).

Although oxygen was being administered during the first 12 hours, a mild hypoxemia was still present immediately postoperatively (see Fig. 1). One to 2 hours later, this supplement was capable of providing normal oxygen saturation levels. At the same time the arterial CO_2 tension was beginning to return to normal levels in the patients of Group A, although it was still not normal the next day. Arterial pH became normal on the day after operation, associated, in Group A, with bicarbonate retention. By the end of the first postoperative week, both groups were hypoxemic (on room air) but had normal CO_2 tensions; a mild alkalosis was in evidence due to retention of bicarbonate.

The course of several of the patients was complicated by the development of significant amounts of nonaerated and/or poorly ventilated lung tissue during the first postoperative week as ascertained at daily physical examination and chest roentgenography. In 8 cases these complications were considered to be more important than in the others. None of these 8 showed atelectasis on the x-ray studies made immediately after operation. Data from these patients are seen in Table III. It should be noted that 6 of them came from Group B in whom little ventilatory dysfunction was found on preoperative pulmonary function studies. The following case report illustrates the changes associated with the development of postoperative atelectasis (Fig. 2).

TABLE III. ARTERIAL BLOOD STUDIES IN 8 PATIENTS WHOSE EARLY POSTOPERATIVE COURSE WAS COMPLICATED BY ROENTGENOGRAPHICALLY DEMONSTRATED REGIONS OF PULMONARY CONSOLIDATION AND/OR POOR EXPANSION. THE MEAN VALUES FOR THESE PATIENTS ARE COMPARED WITH THE MEAN VALUES FOR 8 OTHER PATIENTS WHOSE POSTOPERATIVE RECOVERIES WERE LESS COMPLICATED

PATIENT	GROUP	PREOPERATIVE			WHEN POSTOP. ATELECTASIS FIRST DEVELOPED				ONE WEEK AFTER OPERATION		
		Sa_{O_2}	pHa	Pa_{CO_2}	DAY	Sa_{O_2}	pHa	Pa_{CO_2}	Sa_{O_2}	pHa	Pa_{CO_2}
B. O.	A	91.8	7.49	46	1*	99.0	7.39	59	92.0	7.44	45
L. G.	A	95.3	7.41	42	0	85.1	7.29	51	88.1	7.45	52
T. L.	B	96.5	7.39	43	3	88.6	7.39	37	88.9	7.45	43
R. K.	B	93.0	7.42	41	1*	93.9	7.37	46	85.0	7.48	38
K. G.	B	99.4	7.48	29	1	93.8	7.35	43	95.2	7.43	40
R. N.	B	95.8	7.42	40	4	82.9	7.47	40	92.1	7.45	35
H. S.	B	95.9	7.44	32	2	89.8	7.45	36	90.1	7.46	34
Osb. J.	B	98.1	7.40	39	2	86.5	7.45	43	89.9	7.48	36
Mean		95.6	7.44	39	2	90.0	7.40	44	90.2	7.46	40
Mean for 8 patients without atelectasis		93.7	7.40	40	1	93.1	7.39	43	90.9	7.45	42

*Oxygen administered via nasal catheter.

*The difference of means between the two groups is significant at the 0.01 level.

CASE REPORT

The patient (T. L.) was a 57-year-old man with a tuberculous process in the right upper lobe known to have been present for 26 years. At the time of preoperative evaluation, roentgen studies demonstrated right upper lobe bronchostenosis and atelectasis as well as a small cavity in the superior segment of the right lower lobe and some scarring and bronchial changes in the middle lobe. Both leaves of the diaphragm had low positions but their excursions were good and he denied dyspnea even on heavy exertion.

Spirometric values showed mild ventilatory dysfunction (Table I) and he was judged to be a good surgical risk. Preoperative respiratory gas exchange studies at rest and during moderate exercise on the bicycle ergometer (800 Kg.-M. per minute) showed a mild hypoxemia but no respiratory acidosis. At rest, the shunt-effect equaled 12 per cent of the cardiac output, the dead space-effect was 42 per cent of the tidal volume, and the oxygen diffusing capacity was 8 ml. per minute per mm. Hg per square meter of body surface area.

During operation (resection of the right upper lobe and the superior segment of the right lower lobe), good oxygenation and CO_2 elimination were maintained, including the period of definitive (open) suturing of the bronchial stump. Postoperatively he received oxygen via nasal catheter, resulting in 100 per cent arterial saturation. In the meantime (probably due to hyperoxia), the patient became hypoventilated with the development of a respiratory acidosis and the appearance of small atelectatic areas in the left lower lobe. The blood gas levels returned to normal in the next 2 days and the film, 2 days postoperatively, showed good clearing, although an air bubble was present in the right cupola.

On the third postoperative day the patient complained of dyspnea; he had a stubborn productive cough, and the temperature rose to 40.1° C. on the fourth day. X-ray studies showed the development of a right lower lobe atelectasis and the arterial oxygen saturation fell to 89 per cent. A week later (tenth postoperative day) the atelectasis was still present but it slowly resolved over the next 3 weeks. Antituberculous chemotherapy was continued for 5 months. Ten months after operation the patient was home and feeling well. X-ray studies and his working capacity (better than 900 Kg.-M. per minute) attested to his rehabilitation, and the spirometry and gas exchange studies at rest and exercise showed values which were for the most part as good as or better than the preoperative ones (shunt-effect 9 per cent, dead space-effect 35 per cent, diffusing capacity 6 ml. per square meter).

DISCUSSION

A. *Anesthetic premedication* did not alter arterial oxygenation in any consistent manner. The arterial CO_2 tension rose 4 to 9 mm. Hg in 6 out of those 11 who received the usual morphine-scopolamine or morphine-atropine medication, but did not rise more than 2 mm. Hg in any of the 5 patients receiving a phenothiazine derivative, Lacumin; this finding is in accordance with studies made on other phenothiazine derivatives.[18]

B. *Manually controlled ventilation during the operative period,* using a 3.5:1.5 combination of N_2O and oxygen, resulted in mild hyperoxemia (arterial oxygen saturation 98 per cent), hypocapnia (arterial CO_2 tension 30 mm. Hg mean), and alkalosis (see Fig. 1).

C. *The period of ventilatory arrest during suturing of the open bronchial stump* was not found to be followed by any CO_2 retention or hypoxemia. This was due to the preceding hyperventilation and the insufflation of oxygen.

Sao2
pHa
Paco2
BHCO3
Preoperative
94.2
7.39
43
24
Immediately
postoperative (on O2)
99.6
7.29
47
21
2 days
postoperative
97.2
7.39
38
22

	3 days postoperative	*10 days postoperative*	*10 months postoperative*
$S_{a}O_{2}$	88.6	88.9	96.3
pHa	7.39	7.45	7.39
P_{aCO_2}	37	43	39
$BHCO_3$	21	28	22

Fig. 2.—X-rays and arterial blood values for patient T. L. See text for description.

TABLE IV. MEAN ARTERIAL pH AND CARBON DIOXIDE TENSION LEVELS, BEFORE, DURING, AND IMMEDIATELY AFTER INTRATHORACIC SURGERY (SUMMARY OF LITERATURE)

AUTHOR	SURGERY	POSITION	ANESTHETIC	VENTILATION	PREOPERATIVE		INTRAOPERATIVE		POSTOPERATIVE IMMED.		POSTOPERATIVE 1-2 HR.	
					pHa	Pa_{CO_2}	pHa	Pa_{CO_2}	pHa	Pa_{CO_2}	pHa	Pa_{CO_2}
Gibbon et al.[23] 1950	13 Pneumonectomies 9 Lobectomies	Lateral	Ether, curare	Mechanically assisted	7.38	45	7.23	70	—	—	—	—
Taylor and Roos[24] 1950	6 Pneumonectomies 7 Lobectomies	Lateral	Ether	Respirator or manually assisted	7.42	38	7.21	76	—	—	—	—
Beecher et al.[25] 1951	8 Pneumonectomies 10 Lobectomies	Lateral	Ether, N_2O	Manually assisted	7.40	44	7.31	52	—	—	—	—
Stead et al.[2] 1953	1 Pneumonectomy 10 Lobectomies 7 Segment 2 Wedge	Lateral	Thiopental, N_2O	Manually controlled	7.41	40	7.12	82	7.28	84	—	—
Etsten[26] 1953	8 Pneumonectomies 10 Lobectomies 5 Thoracotomies	Prone	Ether	Spontaneous	7.36	44	7.32	47	—	—	—	—
Siebecker and Curtice[9] 1957	2 Pneumonectomies 3 Lobectomies 8 Segment	Lateral	Succinylcholine, N_2O	Respirator with negative phase	7.42	40	7.36	47	—	—	7.41	40
Holaday et al.[27] 1957	1 Pneumonectomy 1 Segment 1 PDA Ligation 2 Exploratory	—	Cyclopropane	—	7.34	45	7.22	57	—	—	—	45
Clowes et al.[8] 1960	7 Pneumonectomies 23 Lobectomies, segment, wedge 10 Thoracotomies	—	Thiopental, N_2O, Ether	Manually or mechanically controlled	7.40	40	7.33	50	—	—	7.35*	46*
Present series	3 Pneumonectomies 9 3 Segment 4 1-2 Segment	Lateral	Evipan, curare, N_2O	Manually controlled	7.40	42	7.47	32	7.33	49	7.35	46

*3-5 hours postoperatively.

In some other similar cases, not included in this series, increase of pulse rate or blood pressure has sometimes occurred during this period; these changes reversed rapidly if the surgeon manually occluded the open bronchus, so that effective ventilation could be given.

D. *Immediately after operation,* the patients in the minimal dysfunction group had a normal CO_2 tension (42 mm. Hg) whereas alveolar hypoventilation was manifest among the disability group (mean arterial CO_2 tension 55 mm. Hg). The degree of CO_2 retention was greatest in those patients with the worst preoperative ventilatory and lung volume values. A comparison with other series is given in Table IV. That respiratory acidosis can be avoided intraoperatively with manually controlled respiration is quite evident from our series.

The cause of the alveolar hypoventilation immediately after operation is in dispute.[19] Hangover of anesthetic agents is one possibility. A barbiturate (Evipan) was given only in small amounts as induction and could be expected to have been eliminated by the end of the operation.[20] Meperidine, however, was given in repeated small doses during the operation, and some respiratory depressant effect could still be present after the operation; narcotic antagonists might be helpful here.[21] Another likely cause is the rather liberal administration of oxygen via a nasal catheter (2 to 4 L. per minute), leading to relatively high arterial oxygen tensions and a depression of chemoreceptor activity. This factor cannot, however, explain the CO_2 retention, especially when one compares the two groups at the time of the first two postoperative studies, in which the amounts of O_2 given were the same. The CO_2 retention was most pronounced in Group A, in which more segments were resected. Still another factor, probably of importance, is chest pain.

E. *By one day after resection* the pH had returned to normal. This was accomplished in the dysfunction group by a retention of bicarbonate to compensate for the subsiding CO_2 retention. It is likely that the bicarbonate retention is at least partially due to the effect of increased CO_2 tension on the tubular reabsorption of bicarbonate ions.[22] These data are not in agreement with those of Hood and Beall,[19] whose patients were still acidotic 2 to 3 days after operation.

F. *During the first postoperative week* when pain probably becomes the factor leading to inadequate bronchial toilet, atelectasis in association with postoperative hypoxemia was common.[6] But desaturation was also seen in connection with "poor expansion," when the lung was more or less collapsed, hidden behind pleural fluid. What really occurred in the lung in such situations is hard to say. An important change in the ventilation-perfusion relationships, however, is the obvious physiologic consequence. The surprising finding in the present series was that the patients with the better preoperative pulmonary function values were those who more frequently had such complications (Table III). The most likely reason for this paradox is thought to be the special care directed toward the *bad risk cases* on the part of the physicians and staff, such that the maximum benefits of physiotherapy,

bronchial toilet, and other forms of attention were concentrated upon them. In retrospect it is thought that the patients with minimal preoperative dyspnea or pulmonary dysfunction were not adequately trained preoperatively in order that postoperative care and encouragement to cough be successful in bringing up their secretions. Acting on this suggestion, training and care of the more routine cases have subsequently been accentuated, with gratifying results.

G. Patients like those in Group A, with moderate to marked ventilatory dysfunction as manifested by a "maximum breathing capacity" approximately one half that predicted for them and with residual volumes comprising one half their total lung capacities, represent, we believe, the borderline group for extensive resection. "Bad risk" patients in whom ventilatory volumes are worse than these are far less likely to withstand operation even with adjunctive management, including steroid premedication,[28] and artificial ventilation after as well as during operation.[29] Monitoring the arterial blood respiratory gases in borderline as well as bad risk cases provides crucial help in their management.

SUMMARY

1. Patients with reduced preoperative ventilatory function have been followed during pulmonary resection and throughout the critical first postoperative days by means of serial arterial blood studies (oxygen saturation, CO_2 tension, pH). A group of similar size with little dyspnea and dysfunction has been followed for comparison.

2. Patients from both groups did not raise their CO_2 tension when anesthetic premedication consisted of a phenothiazine derivative (Lacumin) as much as when morphine-scopolamine or morphine-atropine combinations were used.

3. Intraoperatively all patients were ventilated by the controlled manual method which provided uniformly low arterial CO_2 tension and high oxygen saturations. No hypoxemia or CO_2 retention resulted from the short period of apnea associated with the definitive closure of the open bronchial stump.

4. Immediately after operation the CO_2 tension rose in all the patients, but only to normal levels in those with good function. The degree of respiratory acidosis which occurred in patients in the dysfunction group correlated with their ventilatory disability as estimated from preoperative spirometry. These patients retained bicarbonate, and a normal arterial pH was present the day after operation.

5. Postoperative difficulties with atelectasis and poor expansion (resulting in significant hypoxemia) were, paradoxically, more common in the group of patients with better preoperative ventilatory function. The factors thought to be responsible for the good results in the ventilatory dysfunction cases include the preoperative training, intraoperative procedures aimed at minimizing function loss, and unflagging postoperative care concentrated upon them.

6. The management of "borderline" and "bad risk" cases is discussed and the role of arterial blood gas monitoring stressed.

Dr. Gösta Birath proposed the subject for investigation and contributed together with Dr. Erik Berglund to the organization of the manuscript. Dr. N. P. Bergh performed the operations and lent his cooperation throughout the study. The personnel of the Pulmonary Function Laboratory contributed greatly, in particular Miss Mary Hansson, Mrs. Berit Tilly, Miss Barbro Göthe, Mrs. Ulla-Britt Almquist, and Miss Anna Gustavsson. The California Tuberculosis and Health Association contributed to defray the expense of medical illustration. Miss Marilyn Lorper performed much of the statistical analysis and Miss Nina Rudolph typed the manuscripts. The investigation was supported generously by a grant from the Swedish Medical Research Council.

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MEDIASTINAL CYSTIC GRANULOMA DUE TO HISTOPLASMA CAPSULATUM

A Report of Three Patients Treated Surgically

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THE VARIED clinical picture of histoplasmosis is gradually being defined as more cases are recognized in the endemic area and, to a less extent, outside of it. Pulmonary lesions predominate; however, the involvement of tracheobronchial lymph nodes has resulted in several clinical entities even when the infection is no longer active. These include superior vena caval obstruction, perforation into bronchi with the formation of broncholiths, compression of bronchi with resultant collapse and bronchiectasis.

Three patients with mediastinal masses, subsequently proved to be fibrocaseous cystic lymphadenitis, have been treated at the Jewish Hospital, Cincinnati, Ohio, in the past 16 months. All three masses were excised and on microscopic examination, *Histoplasma capsulatum* was identified.

CASE REPORTS

CASE 1.—W. W., a 24-year-old woman, was known to have had an asymptomatic mediastinal mass for 2 years. The past medical history was not significant. Physical examination and laboratory findings were within normal limits. A chest x-ray examination revealed two masses, one in the right paratracheal region containing flecks of calcium and the other mass superior and posterior to the calcified portion overlying the upper dorsal spine. Bronchoscopic examination was normal. The preoperative diagnosis was enlarged right paratracheal lymph node and neurofibroma. Thoracotomy was performed on July 27, 1959, and a cystic mass was found adherent to the trachea, upper lobe bronchus, and the superior vena cava. This mass was excised, leaving a small portion of the cyst wall adherent to the trachea.

The postoperative course was complicated by pneumothorax and right pleural effusion, but full recovery ensued.

The gross specimen consisted of a cystic structure 6 by 4 cm. in diameter. The surface was ragged and the cyst contained caseous material in which were irregular fragments of calcium. The cyst wall was grayish-white with focal black discolorations.

Microscopically, there was seen a granulomatous process in the wall with little activity, but there were occasional tubercular structures with epithelioid cells and occasional giant cells of the Langhans type. Calcification was seen in various areas and residuals of lymphatic tissue were observed. No acid-fast bacilli were seen on appropriate stains but, in a few areas, organisms morphologically consistent with *H. capsulatum* were identified.

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CASE 2.—M. T., a 36-year-old white woman, had been under ophthalmologic care for chorioretinitis. A routine chest x-ray study 2 months prior to admission had revealed a calcified mediastinal mass behind the upper portion of the heart, projecting to the right. There was no change in size over a 2-month period. Bronchoscopy was normal. The preoperative diagnosis was mediastinal granuloma, but enterogenous and bronchogenic cysts were also considered. Thoracotomy was performed on Aug. 10, 1959, and the mass was found to be adherent to the esophagus and the right main bronchus. The mass was removed and the patient made an uneventful recovery.

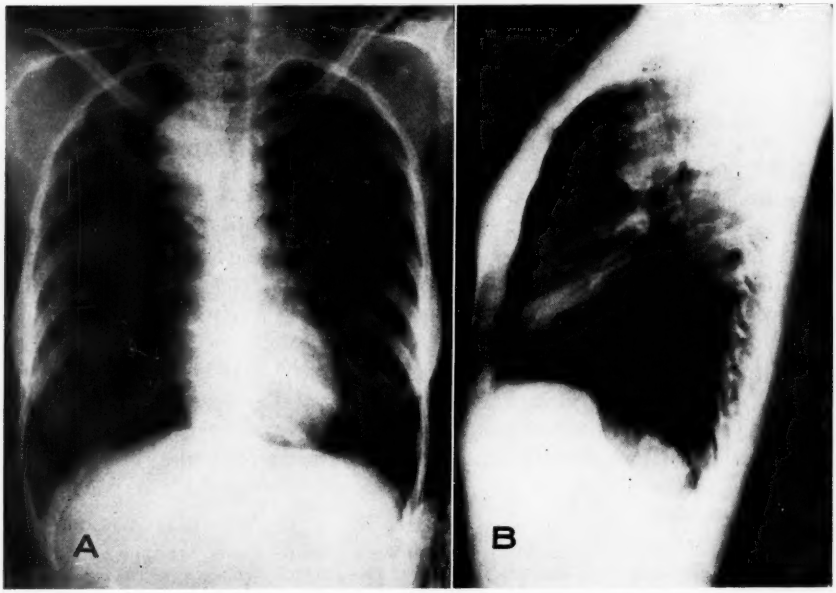

Fig. 1.—Posteroanterior and lateral chest roentgenograms of Case 1. Note the two masses in the right upper mediastinum. One contains flecks of calcium and appears to be in a right paratracheal location. The other lies posterior and superior to the calcified mass and overlies the upper thoracic spine.

Grossly, the tumor was cystic, measuring 6 by 3.5 by 3 cm. The contents were chalky and cheesy in consistency with minute focal calcified concretions, also present in the cyst wall. Microscopically, there was no evidence of inflammatory cell infiltration or organ structure. No acid-fast bacilli were identified on specifically stained sections. Yeast cells, morphologically consistent with *H. capsulatum*, were seen in the sections.

CASE 3.—In June, 1958, T. R., an 18-year-old white boy, was found to have an anterior mediastinal calcified mass, projecting to the left over the aortic arch, in which there had been no change for a 6-month period. The patient was asymptomatic and in good health. Physical examination was normal, as was a routine hemogram. Exploratory thoracotomy was performed on Dec. 5, 1958, and a large irregular mass was found above the left pulmonary artery adherent to the superior vena cava, trachea, and the left main bronchus. This was dissected free and was removed except for a small portion which was adherent to the superior vena cava and left pulmonary artery. The postoperative course was complicated by atelectasis, but the patient made a full recovery.

The gross specimen consisted of three pieces which appeared to represent a broken-down lymph node, with definite cystic character. The cyst wall was heavily calcified.

The microscopic diagnosis was fibrocaseous lymphadenitis with partial calcification. *H. capsulatum* was demonstrated on special stain.

COMMENT

The differential diagnosis of mediastinal masses is difficult and confusing because of the many diseases and developmental anomalies that are commonly known to occur in that area. These include masses due to malignant lymphoma;

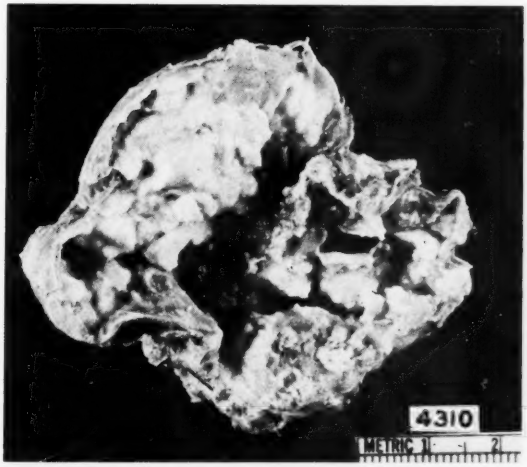

Fig. 2.—Gross specimen from Case 1. This is essentially a cystic structure containing pale caseous material. Irregular fragments of calcification were observed in this.

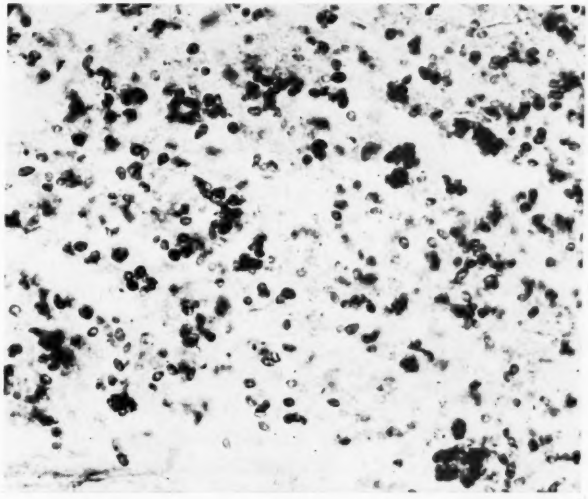

Fig. 3.—Photomicrograph from Case 1. Innumerable organisms, 2 to 5 microns in diameter, are seen, some in clusters (Grocott stain ×1,000; reduced ⅓).

inflammation; nonlymphomatous neoplasms, such as bronchogenic carcinoma, teratodermoids, thymomas and neurogenic tumors; vascular anomalies and aneurysms; gastroenterogenous, pericardial, and bronchogenic cysts; and gastrointestinal hernias and diverticuli. Lyons and his associates,[3] in a review of 782 cases of mediastinal masses, found the largest group to be composed of neoplasms with malignant lymphoma the most common. Inflammatory lesions composed the next largest group which included sarcoid, adenopathy due to infectious mononucleosis, lymphoid hyperplasia, and granuloma due to histoplasmosis, tuberculosis, and coccidioidomycosis.

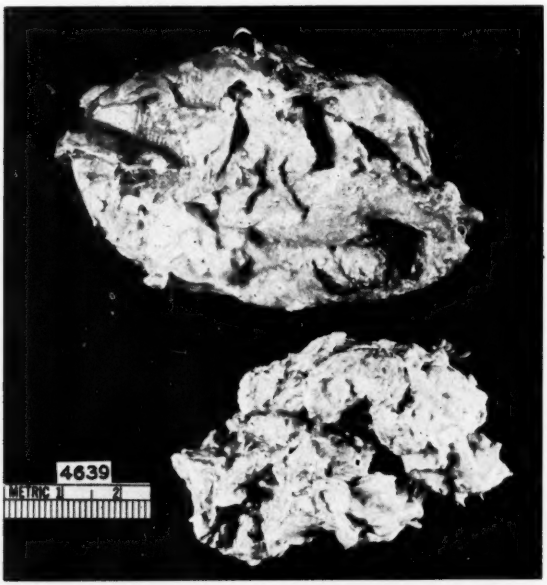

Fig. 4.—Gross specimen from Case 2. This previously opened cystic mass contained both chalky and cheesy material with minute calcifications. The wall was sclerotic with fibrous tags on the surface and focal areas of calcification. The upper specimen is the opened cyst and the lower specimen is the contents.

The incidence of infectious granuloma in the group of mediastinal masses varies from series to series. Lyons and his co-workers found an incidence of 14 per cent.[3] In the experience of Peabody and colleagues,[4] twelve granulomas were observed out of thirty-seven mediastinal tumors and their review of all series to that date demonstrated an incidence of 1.5 per cent.

The awareness of granuloma as a consideration in mediastinal "tumors" is relatively recent. Grace, in 1942, was the first to report the surgical excision of tuberculoma of the mediastinum. Since that time, numerous reports of granulomas presenting as mediastinal masses have appeared.[1-5, 7, 8]

Frequently, the etiology of these granulomas was considered to be tuberculous. In 1954, Kunkel and his co-workers[2] expressed the view that these lesions should be called mediastinal granulomas rather than "tuberculomas"

since tubercle bacilli were seldom demonstrated by culture or microscopic section. In 1958, Peabody and his associates[5] reported the first case of culturally proved tuberculoma of the mediastium, and in their review of all previous resected "tuberculomas" found only one in which the tubercle bacillus was seen microscopically. Soon after this, Karlson[1] reported 19 cases of which 3 were proved to be tuberculous by culture and 1 in which there was demonstrable acid-fast bacilli by microscopic examination.

Samson[7] first incriminated *H. capsulatum* as a cause of mediastinal granuloma in 1955. In 1958, Peabody[4] demonstrated *H. capsulatum* in 5 of 12 cases by use of PAS and methenamine and silver nitrate stains. Karlson found *H. capsulatum* in 1 of his 19 reported cases. Histoplasmosis was listed as the etiological agent in 53 instances by Lyons and his co-workers.[3] The criteria used to establish that diagnosis were not elucidated.

Peabody and his associates[4] found *H. capsulatum* only in areas of caseous necrosis and believed that the inability to demonstrate the organism in granuloma, composed mainly of fibrous tissue, did not eliminate the possibility that it represented residual "burnt-out" histoplasmic foci. They believed that histoplasmosis was a more common etiological factor than commonly supposed since, in their reported cases of solitary pulmonary granuloma, 53 per cent were due to *H. capsulatum.*

The demonstration of *H. capsulatum* in the three mediastinal granulomas reported here is not surprising. Straub and Schwarz[9] reviewing 105 consecutive autopsies in this endemic area demonstrated *H. capsulatum* in 70 cases with healed primary complexes. It is of interest and importance to note that in all cases reported here special stains were necessary to identify the etiological organisms and, in another, a definite etiology was not established until careful re-examination of new sections was done.

Mediastinal granuloma, in general, regardless of etiology, may be solid, composed of active granuloma with epitheloid cell tubercles, Langhans' giant cells with central caseation, solid with cystic degeneration, or, as in the cases reported here, primarily cystic with a wall composed of fibrous tissue and a paucity of palisading histiocytes or giant cells. Calcification is often noted in the cyst wall. The cystic form is not unusual and has been described previously.

The preoperative diagnosis of mediastinal granuloma may be difficult because of the necessity for differentiation from other tumors occurring in the mediastinum. As seen in the cases reported here, aids in diagnosis are the discovery on routine chest x-ray studies of the occurrence in young people, and the predominance of a right paratracheal location with visible calcification. However, in other reports and in these cases, teratoma, neurogenic tumors, bronchogenic and enterogenous cysts were frequent preoperative diagnoses. The importance of pulmonary parenchymal calcification as an aid in diagnosis would not seem of value in this endemic area since the incidence of pulmonary calcification is higher in the general population.

While this lesion is benign, most authorities recommend removal of as much of the "tumor" as possible.[1, 2, 5, 6] The indications for surgery are the

inability to make a completely accurate diagnosis without thoracotomy, the danger of subsequent rupture of an existing cyst which would lead to mediastinitis and its attendant sequelae, and the impingement on mediastinal structures by the mass itself.

A follow-up on the 3 cases reported here reveals that Case 1 was well 5 months after operation and Cases 2 and 3 were asymptomatic without evidence of recurrence at 10 and 17 months, respectively.

Follow-up data are sparse on previously reported cases. Karlson and Timmes[1] reported 19 cases of surgically treated mediastinal granuloma followed up to 9 years. In 4 cases, tubercle bacilli were demonstrated microscopically or by culture and in 1 *H. capsulatum* was demonstrated. No etiological organism was found in the remainder. Antituberculous chemotherapy was instituted in the cases in which tubercle bacilli were demonstrable. Seventeen patients, including those with granuloma due to histoplasmosis were asymptomatic at 9 years, but 2 patients in whom the etiology could not be determined developed active tuberculosis during the follow-up period. On the basis of these findings, it was thought that all patients in whom fungus was not demonstrated should have antituberculous chemotherapy postoperatively. The 3 cases reported here and the case above are the only published follow-ups of mediastinal granuloma due to *H. capsulatum*. It would appear that specific chemotherapy is not indicated postoperatively since no instances of pulmonary or disseminated histoplasmosis have been seen after removal of the granuloma. This may be related to the fact that demonstration of the organism in microscopic section does not denote viability in the case of *H. capsulatum*.

SUMMARY

Three cases of cystic mediastinal granuloma due to *Histoplasma capsulatum* are reported. This is a relatively rare entity, but increasing awareness and the use of special stains may demonstrate that this organism is not an uncommon etiological agent of mediastinal granuloma, especially in endemic areas.

Mediastinal granuloma must be considered in the differential diagnosis of mediastinal masses and, although clinical features may be very suggestive, excision is usually required for confirmation of the diagnosis and definite therapy.

We wish to thank Dr. Leonard Gottesman for permission to report Cases 2 and 3 and Dr. Sanford Blank for permission to report Case 1 in this study.

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SURGICAL EXPERIENCES WITH PULMONARY COCCIDIOIDOMYCOSIS

A Survey of 112 Operative Cases

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A CONTINUING INTEREST[1, 2] in coccidioidomycosis has persisted over the years at this Center, principally because many of our patients, transient in the southwest United States, have contracted this disease and have been transferred here for treatment. Since the second World War, an appreciable group of patients have undergone various forms of medical and surgical treatment here for this disease. The frequency of the employment of surgery in treating this disease has increased steadily since our first operative case in 1947. This increase here, as well as elsewhere, has paralleled the development and increasing scope of thoracic surgery, particularly in those pulmonary diseases for which as yet no completely effective chemotherapy exists.[3, 4]

Patients who have been operated upon for coccidioidomycosis have been selected for various reasons. The commonest indication has been the presence of symptomatically proved lesions, particularly cavities, for which no other effective treatment is available. Another firm indication has been the presence of symptomatically proved or unproved cavitary disease. In both the above instances operation has been directed toward excising localized disease and the return of individuals to full activity, clinically well with clear x-ray pictures. Our primary purpose was to avoid the later complications of cavitary disease such as enlargement, rupture, bleeding, and infection. Many of our patients have been operated upon solely because of undiagnosed pulmonary lesions. In these patients the diagnosis has been made, rational treatment given, and disposition afforded. A few of our patients have been operated upon because of spontaneous rupture of cavities with resulting empyema and bronchopleural fistula. At this time a rather long follow-up and, perhaps, improved perspective prompts the review of these cases.

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This review does not imply any indorsement of the opinions advanced or any recommendation of such products as may be named.

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ANALYSIS OF CASE MATERIAL

One hundred and twelve patients have been operated upon at this hospital for pulmonary coccidioidomycosis. Ninety-seven have been male, of whom 5 were Negroes, 3 Orientals; the remaining 15 were females.

Fifty-six of the patients were operated on for predominantly cavitary disease and 53 for nodular or granulomatous infiltration. Three underwent operation for empyema and bronchopleural fistula due to ruptured cavities.

Of interest is the fact that 26 (46 per cent) of the patients with cavitary disease were symptomatic on admission, 14 (26 per cent) of the nodular or granulomatous group were symptomatic, and 3 patients with ruptured cavities, empyema, or bronchofistula, were symptomatic also. Thus, 43 out of 112 (38 per cent) were definitely ill on admission for therapy. Symptoms were varied and are recorded in Table I.

TABLE I

1. Cough and sputum production	26
2. Chest pain	16
3. Hemoptysis	8
4. Symptoms of acute pneumonia	4
5. Symptoms of pneumothorax and empyema	3
6. Weight loss, severe	2

Skin testing revealed an appreciable group of patients who did not react positively (Table II).

TABLE II. SKIN TESTS

	TOTAL CASES	POSITIVE	NEGATIVE	NOT RECORDED
Cavitary disease	56	42	12	2
Nodular disease	53	35	12	6
Bronchopleural fistula and empyema	3	2	0	1

Serological tests for coccidioidin have been fairly regularly recorded throughout the series. However, because of a lack of consistency of results this test has not been considered of great value or important diagnostic help surgically. Positive cultures of resected specimens and sputa have been frequent (Table III).*

TABLE III. CULTURES POSITIVES

	RESECTED LESION	SPUTA
Cavitary disease	37	9
Nodular disease	15	1

Operative procedures performed are listed in Table IV. When a complication occurred as a result of surgery, it is listed by the type of operation performed.

*All pathologic specimens have been confirmed by the Armed Forces Institute of Pathology for correctness of pathologic diagnoses.

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TABLE IV

	CAVITARY LESION	COMPLICATION	NODULAR LESION	COMPLICATION	BPF AND EMPYEMA	COMPLICATION
Lobectomy	20	4	1	1	—	—
Lobectomy, decortication and thoracoplasty (tailoring)	1	0	0	0	—	—
Segmental resection	20	8	5	1	—	—
Wedge resection	15	0	47	5	—	—
Decortication and wedge resection	—	—	—	—	3	2
Totals	56	12	53	7	3	2

Twenty-one complications occurred in 112 operations. There was no operative mortality in the series. In 11 of the complicated cases, operation was performed by residents and in 10 by senior surgeons. A list of 21 operative complications related to the type of surgical procedure and type of disease is seen in Table V.

TABLE V

COMPLICATION	OPERATION	CAVITARY DISEASE	NODULAR DISEASE	EMPYEMA AND BRONCHOPLEURAL FISTULA
1. Postoperative effusion, small	Lobectomy	x		
2. Postoperative pneumothorax (questionable recurrent cavity)	Segmental resection	x		
3. Postoperative pneumothorax	Lobectomy		x	
4. Postoperative pneumothorax	Segmental resection	x		
5. Moderate pleural reaction	Wedge resection		x	
6. Moderate pleural reaction	Segmental resection	x		
7. Moderate pleural reaction (probable abscess of lung and pneumothorax postoperatively)	Wedge resection		x	
8. Postoperative effusion, small	Decortication and wedge			x
9. Persistent leak	Lobectomy	x		
10. Persistent leak	Decortication and wedge			x
11. Persistent leak	Segmental resection	x		
12. Persistent space (questionable recurrent cavity)	Segmental resection	x		
13. Persistent space	Wedge		x	
14. Persistent space	Segmental resection	x		
15. BPF and empyema	Segmental resection	x		
16. BPF and empyema	Lobectomy	x		
17. Space and empyema (later recurrent cavity)	Segmental resection	x		
18. Atelectasis	Segmental resection		x	
19. Atelectasis and later homologous serum jaundice	Lobectomy	x		
20. Hemothorax	Wedge resection		x	
21. Hematoma, lung	Wedge resection		x	

It is notable that all patients with complications recovered and x-ray studies showed clearing after treatment for these developments, with the exception of 4 on whom brief summaries are included in our follow-up analysis.

The follow-up review of these patients has been rewarding. Only 4 of our patients have been lost to follow-up after discharge; these had all undergone successful, uncomplicated operation. Six of our patients have been operated upon recently (within 1½ years) and although perfectly well after uncomplicated operation, they have been excluded from our follow-up review because of the recentness of the operation. The remaining 102 patients have been followed an average of 5.6 years. The earliest time of operation in this group was in 1947 and the latest in 1958. All of these patients are well and at gainful employment, except for the following 4 cases of complications which are reported below. The results in these instances have not been satisfactory.

1. A 22-year-old Negro underwent a segmental resection of the left upper lobe for cavitary lesion in April, 1954. He was discharged with a small residual apical space. Follow-up study of this patient revealed that he had periodic small hemoptyses and chronic cough as late as 1957 when he was lost to follow-up examination. It is thought this patient undoubtedly would have had a better postoperative course if the space problem had been eliminated early in his postoperative course, perhaps by a tailoring thoracoplasty.

2. A 31-year-old white man was admitted in 1946 with a history of recurrent right chest pain since 1940. An acute febrile episode associated with dyspnea and pleuritic pain prompted admission. He was found to have a ruptured cavity with a pyopneumothorax. Decortication and surgical excision of the lesion in 1947 did not correct the fistula. A thoracoplasty was performed with improvement. The patient suffered a persistent chronic cough and occasional small hemoptysis until his death in 1956 of a heart attack. This patient was not cured of his disease, although a 10-year follow-up study was quite long. In retrospect, more radical surgery after initial surgical failure might have improved the result.

3. A 30-year-old white male patient underwent an anterior segmental resection of the left upper lobe and a subsegmental resection of the upper lingula in late 1956. This was followed by a space, empyema, and fistula problems. A completion lobectomy and tailoring thoracoplasty followed in March, 1957. However, a bronchopleural fistula persisted and recurrent cavitation was noted. Amphotericin B was given, producing negative sputa. A completion pneumonectomy was done in October, 1957. Amphotericin was continued postoperatively. In 1959, the patient was well and only slightly limited by loss of the left lung. This case illustrates the danger of persistent space problems and presence of pleural contamination.

4. A 43-year-old white male patient underwent a left lower lobectomy in 1949 for symptomatic left lower lobe cavitary disease that had been present for over 6 years. His postoperative course was complicated by a bronchopleural fistula which healed. One year later, because of x-ray evidence of bronchiectasis

in the lingula, a resection of the segment was done in another hospital. At this time, evidence of infection was found about the left lower lobe stump. In 1955, the patient developed a mediastinitis which was due to coccidioidomycosis; this was treated. The problem was complicated by bronchopleural fistula. Three stages of thoracoplasty were done in 1956. A Schede thoracoplasty was done in 1957. In 1958, Amphotericin treatment was given for the fistula, which the patient still has. However, in 1960, the patient is still carrying on fairly well despite the fistula. It is difficult to reconstruct the surgical error in this case. One presumes disease must have been present in the lower lobe bronchus at the time of original resection and closure.

Amphotericin B has been used in 8 patients. We have been attracted to its use because of recent observations by our medical colleagues who have found that it regularly produces negative sputa in cavitary cases, although often little clinical or other objective improvement has been observed in the patient. They have similarly noted that sputa again became positive after treatment was stopped.

Four patients recently operated upon with cavitary disease were treated preoperatively to the point of sputum conversion, and convalesced nicely under postoperative treatment with Amphotericin B. One of these patients had undergone a wedge resection and 3 had had segmental resections.

One patient with a small apical space following apicoposterior segmentectomy of the left uppper lobe was treated prophylactically with Amphotericin. His course was uneventful and the space obliterated spontaneously.

Another patient who developed a persistent apical space after surgical resection of a cavitary lesion, right upper lobe, was found at the same time to have a positive sputum culture for *Coccidioides immitis.* A suggestion of a new cavity was seen in the remaining right upper lobe on x-ray. This space was treated by intubation and suction. A course of Amphotericin B was given with no change in the x-ray appearance or recurrence of positive sputum. One year later the x-ray appearance was normal and the patient was on full activity.

Two other patients received Amphotericin B therapy. Both have been previously discussed under complications. In neither instance did we find good reason to believe that Amphotericin B favorably influenced the course of these patients beyond producing negative sputa.

Thus, a total of 8 patients have received Amphotericin therapy with questionable but suggestive evidence of value.

DISCUSSION

In reviewing our criteria for operation it appears that removal of cavitary coccidioidal lesions is fully justified and indicated. The frequency of symptoms and the occasional complications of cavitary disease fortify this position. The 5-year follow-up study of patients not operated upon shows evidence of difficulty in at least 20 to 30 per cent of cases.[5]

We have been impressed by the fact that space or leak problems postoperatively have given the greatest morbidity. We have had a few more after segmental resection than after other operations. It is apparent that this major

problem in the postoperative period must be promptly solved and the space obliterated to avoid empyema, fistula, recurrent cavitation, and spread. As many cavitary lesions involve segmental planes, erring on the side of lobectomy in occasional cases may avoid contamination and may also obviate a persistent leak or space problem. This is a problem associated with segmental resection, whether performed for coccidioidomycosis or any other inflammatory condition.

It is difficult to assess the value of Amphotericin B as an adjunct to operation for coccidioidomycosis from our small experience in 8 cases. While we have regularly seen it produce negative sputa preoperatively in cavitary cases, we have been able to grow the fungus with ease from the resected cavities in each instance in which it has been used. Certainly it is not a fully effective fungicidal preparation. However, it may afford some protection when contamination of the pleural space has inadvertently occurred in a segmental resection, for example. For this reason additional trial may improve our surgical results.

SUMMARY

A review of our surgical experience in patients with coccidioidomycosis has been presented and discussed. Resection of cavitary disease is urged in an attempt to eliminate symptoms, avoid complications, and gain an acceptable therapeutic end result. It is believed that proper attention to the details of surgical technique can obviate many of the reported complications. A small experience with adjunctive Amphotericin B therapy has been discussed.

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MEDIASTINOSCOPY

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In 1959, Carlens presented a method for direct examination of the anterior part of the mediastinum. This was accomplished with a specially designed mediastinoscope which was introduced through an incision in the jugular fossa in the midline. The tissues above the trachea were first separated with a finger, and the ventral surface of the trachea was followed down to the carina with the mediastinoscope. The examination provided data of the tracheal region and of both main bronchi; biopsies could be taken of the lymph nodes, or, in cases of direct mediastinal extension of the tumor, from the tumor tissue itself.

The immediate appeal of Carlens' method lies in its relative safety as compared with other methods in which the mediastinal examination is started laterally in the neck and not in the midline. In careful hands the examination can be expected to proceed without complications which, as a form of pneumothorax, might be quite considerable in the lateral approach.

Although the methods for diagnosing pulmonary cancer are continually improving, the selection of patients suitable for operative procedures still presents considerable difficulty. The number of exploratory thoracotomies still represents quite a high figure in the statistics for cases of operation, and the same applies to the so-called palliative resections. It is evident that the exploration of patients with inoperable pulmonary carcinoma shortens the patient's expectations of life by many months. In addition, an unnecessary operation places the patient in the hospital for many weeks; and an exploratory thoracotomy also frequently gives an impetus to a rapid progression of the disease.

In the evaluation of operability, all saving examination methods should be employed, such as bronchography and bronchoscopy, tomography, pneumomediastinography, and scalene node biopsy. Among these nonstressing methods, mediastinoscopy can well be included. With the above points in mind, and having heard of Carlens' success with mediastinoscopy, we decided to try it in the common effort of the Clinics of Surgery and of Otolaryngology which work together in the evaluation of cases of intrathoracic disease.

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EARLIER STUDIES OF MEDIASTINOSCOPY

The original report of Carlens is based on experience with mediastinoscopy in the Karolinska Hospital, Stockholm. His series consisted of over 100 cases and the procedure did not cause any complications. Mediastinoscopy proved a means of excluding from major surgery cases of mediastinal carcinoma extension, and it provided direct knowledge of an intact mediastinum in patients otherwise thought to be inoperable. Lymph node biopsies could be obtained also in cases not definitely diagnosed by other means.

All patients were examined under intubation anesthesia, and they were able to leave the hospital in a few days after mediastinoscopy. Sulfapenicillin powder was insufflated into the wound and no postoperative infections were reported.

In Finland, Seppälä has given a short account of his experience in 32 cases of mediastinoscopy at Kivelä Hospital, Helsinki. He stresses the importance of the method, especially in evaluation of cases of carcinoma and in differential diagnosis.

MATERIAL AND METHOD

The present material consists of 44 patients treated at the Clinic for Thoracic Surgery for various reasons. In the majority of these patients the diagnosis of pulmonary carcinoma was already established, and mediastinoscopy was performed to evaluate operability. In a smaller number of cases, diagnosis could not be reached preoperatively and mediastinal examination was made in the hope of getting additional data.

All mediastinoscopies were made at the Department of Otolaryngology by the otolaryngologist (T. P.), while the general thoracic evaluation and all thoracotomies or pulmonary operations were made by the thoracic surgeon (S. V.). There was close cooperation throughout the work. This was greatly facilitated by the fact that the two departments adjoin each other.

The apparatus used for mediastinoscopy is basically the same as the one designed by Carlens and manufactured by Stille Company, Stockholm. We have added to the armamentarium a few ordinary, endoscopic forceps for more accurate removal of small pieces of tissue for biopsy. Our equipment includes two needles with a long shaft which can be used as such, or connected to a tuberculin syringe for puncture and aspiration of tissues suspected for some reason to contain a blood or fluid filled structure, such as an arterial aneurysm, a larger vein, a hemangioma, or some other type of cystic tumor. A biopsy without preliminary needling might prove disastrous in some of the cases just mentioned.

The tissue dissector of Carlens, equipped with small sponges in the tip, was mainly used for spreading the tissue planes apart around the carina. The suction tips can also be used effectively for this purpose. If a biopsy is to be taken from a lymph node, this is first dissected as free as possible with the suction tip; if the gland is not fixed it can generally be removed in toto with the forceps.

The bleeding after biopsy can best be controlled with a gauze pack. Small amounts of Adrenalin can be used but care should be taken not to use it excessively, as the drug is easily absorbed and causes fluctuations in blood pressure. Finally, the bleeding area, or the area of biopsy, was covered with a slice of Gelfoam, soaked in Neotracin, and left in place. This has the advantage of stopping all minor bleeding; furthermore, if the biopsy has been taken from a direct carcinomatous extension, the Gelfoam becomes glued to the biopsy surface and so prevents dissemination of tumor cells into the open parts of the mediastinum.

Silver clips, as used by Carlens, could equally well be applied to the bleeding point, if this can be accurately determined. The clips have the additional advantage of showing the exact site of the biopsy in the postoperative roentgen films.

All operations were made under intubation anesthesia since, obviously, local anesthesia is less suitable for work in the thorax. Supronal powder was insufflated into the wound at the completion of the operation. No drains were used.

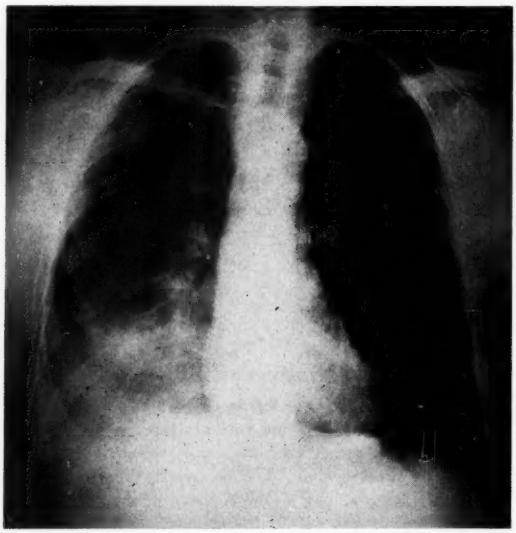

Fig. 1.—Case 1. Carcinoma of the right lower lobe with one verified metastatic node.

RESULTS

In 15 instances of 33 cases of pulmonary carcinoma, mediastinoscopy disclosed carcinomatous infiltration of the mediastinal lymph nodes. In some of these, metastatic involvement of the mediastinum was also apparent by ordinary examination methods. However, the incidence of positive findings at mediastinoscopy must be considered high, as those patients in whom the disease was primarily judged inoperable were not subjected to mediastinoscopy.

In addition to the paratracheal lymph nodes, the nodes caudal and anterior to the bifurcation are easily visible at mediastinoscopy. It is known that these glands often are invaded by metastases in pulmonary carcinoma; in this material the incidence was 35 per cent. Small, mobile metastases in this region can be removed at the resection; however, if the mediastinoscopy disclosed a large, fixed metastatic mass under the carina, with fixation of the main bronchus, the patient was considered inoperable. Sometimes a high primary tumor, in the main or in the upper lobe bronchus, could be seen at mediastinoscopy as the bronchial wall had become destroyed by the tumor. In many cases a large part of the tumor could be palpated with the finger, and precise knowledge could be obtained of operability.

Two case histories of patients included in the series are presented.

CASE REPORTS

CASE 1.—(O. N., No. 392/60). A 47-year-old man with slight hemotypsis had had repeated pneumonic infiltrations for 3 to 4 months. Sedimentation rate was 60 mm. per hour. Roentgen examination showed a shadow with pneumonic infiltration in the right lower lobe (Fig. 1). At bronchoscopy, tumor tissue was found to fill the orifice of the superior lower lobe bronchus; biopsy showed a microcellular carcinoma. The trachea was normal and the bifurcation thin and mobile.

At mediastinoscopy, palpation with the finger disclosed no abnormality. A pea-sized lymph node was seen at the lower end of the trachea and removed. There were no suspicious nodes at the bifurcation. The histologic diagnosis of the removed node was metastatic spread of the microcellular carcinoma. Apart from the lymph node metastasis, operability seemed good.

Fig. 2.—Case 2. Carcinoma of the right upper lobe with large mediastinal extension.

At pneumonectomy, no other paratracheal or subcarinal lymph nodes were found, and it was thus easy to divide the main bronchus and to tie and cut the pulmonary artery. The lower lobe was largely destroyed by the tumor and there were enlarged lymph nodes around the pulmonary vein. Histologically these presented no carcinomatous involvement.

The patient in this case had microcellular carcinoma of the right lower lobe. Mediastinoscopy disclosed one metastatic paratracheal lymph node but no other suspicious lesion. These findings were confirmed by successful surgery.

CASE 2.—(M. J., No. 2423/60). The patient was a man of 47 years of age who had had slight fever and fatigue for 4 months. Roentgen examination showed an atelectasis of the right upper lobe (Fig. 2).

Bronchoscopy disclosed carcinoma in the orifice of the right upper lobe. The carina was thin and the bifurcation was easily movable. Roentgenologically and bronchoscopically this spinocellular carcinoma appeared operable.

A hard, tumor-like formation was found at mediastinoscopy close to the take-off of the common right upper lobe bronchus, and continued upward on the right side of the trachea for 3 cm. This infiltration consisted partly of carcinoma proper and partly of hard lymph node metastases. On the bifurcation and around the left main bronchus there were evident tumor metastases. Biopsies of all these locations showed metastatic carcinomatous infiltration. On the basis of these findings the tumor was considered inoperable.'

Thus, the patient in this case had right upper lobe carcinoma which seemed operable by ordinary examination methods, yet mediastinoscopy showed extensive carcinomatous mediastinal involvement which rendered the patient inoperable.

Discussion.—The remaining 11 patients had a variety of nonmalignant diseases. In 8 cases an exact diagnosis could be reached by mediastinoscopic examination. All cyst-like formations were readily diagnosed with needle puncture and aspiration; if the palpating finger felt anything suggestive of malignant degeneration, biopsies were obtained to disclose the nature of the process.

In sarcoidosis the violet color of the lymphatic tissue and the abundance of this tissue around the carinal region, as well as its softness and homogenous nature, is pathognomonic for this disease and makes the diagnosis obvious even macroscopically. Touched with instruments, the glands bleed diffusely, but this is easily controlled with pressure.

In tuberculous involvement there were no clear-cut macroscopic changes; the lymph nodes were generally medium sized and one could at times obtain cheesy material from within the gland. However, two large carcinomatous glands in this series also contained similar material. Many tuberculous patients presented adhesive and fibrous changes around the bifurcation; the preparation of tissues and the technique of mediastinoscopy demanded greater care than usual.

COMPLICATIONS

In no case was there any bleeding after mediastinoscopy; nor were there any pleural ruptures. The recurrent nerve, although quite often seen on the left side, remained intact in all cases. The patients were in a good general condition postoperatively and were able to leave the hospital in a few days, if mediastinoscopy was the only procedure performed.

In 1 case, a man 58 years of age, cardiac arrest developed postoperatively after the patient had waked up and the intubation tube had been removed. Heart massage given immediately after left-sided thoracotomy, combined with electric shocks, restored the heartbeat in less than half an hour. During the massage a large, old scar of an earlier infarct was seen in the posterior wall of the left ventricle. The postoperative electrocardiogram showed signs of a new infarct, but these changes disappeared after 2 weeks. The patient regained his previous condition in the course of a couple of months. The primary reason for the cardiac arrest remains obscure, but we strongly suspect that a new coronary thrombosis developed postoperatively.

COMMENT

Mediastinoscopy is of particular value in that it gives information of the nature of the lymph nodes situated (1) paratracheally, (2) caudal to the bifurcation in the anterior mediastinum, or (3) anterior or lateral to the main bronchi to the level of the upper lobe bronchi. Laterally one can examine the areas around the aortic arch and the azygos vein. It should be stressed that the metastases or processes at the posterior mediastinum remain outside the field of the mediastinoscope. Naturally, the lower part of the anterior mediastinum below the upper lobe bronchi is inaccessible to the mediastinoscope.

Paratracheal metastases, if present, are generally easily seen at mediastinoscopy. They can always be palpated with the finger, even in the initial phases of the examinaiton, as the tissues are separated above the trachea to allow passage of the mediastinoscope. These hard glands are often solitary, sometimes in chains, and often mobile. They can be dissected free with the suction tip and removed in toto during the examination. They can also be removed during the resection operation if the primary tumor is operable and the region of the bifurcation is free from fixing metastases.

Often the glands involved are small and do not yet cause broadening of the mediastinum in the roentgen film; nor can they be seen on pneumomediastinography. Direct inspection with the mediastinoscope and a later histologic examination of the specimens give the thoracic surgeon important additional information.

It is clear that, during mediastinoscopy, one has to work in an area where there may be carcinomatous tissue. However, generally there is a question of biopsies from metastatic lesions which can be removed in toto. Even if direct carcinomatous extension is biopsied, we believe that sealing off of the excision area with slices of Gelfoam prevents the loose-cell spread into the open part of the mediastinum. None of our patients have shown rapid progress of the disease after mediastinoscopy as is sometimes seen after greater explorative operations.

The procedure is essentially without danger if the surgeon bears in mind the few danger points: the mediastinoscope must be kept in midline; in left-sided expansive processes the recurrent nerve is very close to the midline; when approaching the left upper lobe bronchus the large vessels must be carefully watched. It also seems advisable to puncture and, possibly aspirate, vessel- or cyst-like structures before an actual biopsy is made.

It seems to us that mediastinoscopy is a valuable adjunct for the thoracic surgeon in those cases especially in which the operability remains in doubt. It can also solve some pulmonary problems by providing a clear-cut histologic diagnosis in cases where other conventional methods have failed. We feel sure that mediastinoscopy will become a permanent, useful, nonstressing examination method in thoracic clinics and an excellent diagnostic aid in selected cases.

The financial support by the Sigrid Jusélius Foundation is gratefully acknowledged.

SUMMARY

Experience is reported on 44 patients with intrathoracic diseases in which mediastinoscopy, using Carlens' approach, was performed. By providing histologic material from mediastinal lymph nodes or tumors, the examination gives exact data of the nature and extent of the process in the anterior mediastinum. The operative indications in pulmonary carcinoma are better defined, and many patients with advanced mediastinal involvement are spared explorative thoracotomy. In our cases there were no complications due to mediastinoscopy, and in careful hands the procedure seems to involve very little risk. The authors feel that mediastinoscopy will become a standard procedure in thoracic clinics.

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EXPERIMENTAL STUDIES OF INTRAPLEURAL INJECTION OF SODIUM HEPARIN IN PNEUMONECTOMIZED DOGS WITH AND WITHOUT INFECTION

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THE TREATMENT of post-pneumonectomy empyema still remains unsatisfactory. The antibiotics have proved to be very helpful in treating this complication, but their effectiveness is limited. The formation of adhesions with multiloculation of infected fluid prevents equal distribution of antibiotics, given either systemically or locally. Moreover, under these circumstances, the effectiveness of antibiotics is apparently limited even when they do reach the site of infection because the infectious organism (being in static phase with low metabolic rate) is often relatively resistant.[1] Second, the leukocytes concentrated in loculated pus pockets, because they are largely degenerated, have little capacity to provide an effective phagocytic defense to supplement the action of antibiotics.[1]

The use of fibrinolytic enzymes in total empyemas also has not proved to be fully satisfactory.[6-11] The side effects, such as hyperthermia, hypotension, etc., and the limited or absent fibrinolytic action in a good percentage of cases, especially in those in which there is cellular organization of the contents of the chest cavity, seriously limit their usefulness.

Relief by surgical drainage, either open or closed, on the other hand (which is certainly the treatment of choice in abscesses or empyemas), may be hampered by the presence of multiple adhesions and extensive loculation of the infected fluid.

This experiment was conceived to evaluate the influence of intrapleural injection of sodium heparin on the formation of adhesions in the hope that it might prove to be helpful in developing more satisfactory prophylaxis and management of potential or actual empyema in a contaminated pleural space.

MATERIAL AND METHODS

Thirty-eight healthy mongrel dogs, weighing from 9 to 14 kilograms, were used. Anesthesia was induced with intravenous sodium pentobarbital (30 mg. per kilogram)

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and respiration was controlled by intermittent positive pressure with air through an intratracheal tube. The procedures were performed with aseptic technique and in each case the right hemithorax was entered through the fifth interspace and right pneumonectomy was performed. The bronchial stump was closed carefully with silk sutures and covered with pleura. The animals were divided into three groups:

Group A.—Pneumonectomy was performed in 15 animals. Seven served as controls and received no heparin. The remaining 8 dogs received sodium heparin intrapleurally, 3 mg. per kilogram, beginning 24 hours after the pneumonectomy and continuing every 12 hours until the dogs were sacrificed 6 to 55 days later.

Group B.—Pneumonectomy and pleurectomy were performed in 10 dogs. In each instance the parietal pleura was removed and the chest wall was scraped with a curette and rubbed vigorously with gauze. Five of the dogs were given sodium heparin intrapleurally, 3 mg. per kilogram body weight, starting 24 hours after the pneumonectomy and then this dosage was continued afterward intrapleurally every 12 hours until the dogs were sacrificed 5 to 30 days later. The remaining 5 animals received no sodium heparin.

Each animal in Group A and Group B was given 300,000 units of penicillin and 1 Gm. of streptomycin intramuscularly daily for the first 5 days after pneumonectomy.

Group C.—Pneumonectomy and pleurectomy were preformed in 13 dogs and the right pleural space was contaminated at the time of operation in 9 animals with 0.5 c.c. of a 24-hour-old broth culture of coagulase-positive *Staphylococcus aureus,* nonsensitive to penicillin and streptomycin; each cubic centimeter contained 400 million colonies. In the remaining 4 animals, the pleural space was contaminated with 1 c.c. of a 24-hour-old culture of pneumococcus, each cubic centimeter contained 200 million colonies. Six of the dogs in this group received sodium heparin in the same dosage as those in Groups A and B, and the other 7 received none. One of the control dogs and one of those which received heparin were given 1 c.c. of Chloromycetin intramuscularly, daily, for the first 5 days. Two of the animals which received heparin and 3 of those which did not receive heparin were given 300,000 units of penicillin and 1 c.c. of streptomycin intramuscularly daily for the first 5 days. The remaining animals did not receive antibiotics. Clotting times (three tube method) were done in most of the animals which received heparin before the administration of each dose and were found to be within the 10 to 20 minute range. No animal showed any sign of abnormal bleeding in the postoperative period.

TABLE I. PNEUMONECTOMY

NONHEPARIZED GROUP				HEPARINIZED GROUP			
DOG NO.	SURVIVAL (DAYS)	ADHESIONS IN CHEST CAVITY	OTHER CONTENTS OF THE CHEST CAVITY	DOG NO.	SURVIVAL (DAYS)	ADHESIONS IN CHEST CAVITY	OTHER CONTENTS OF THE CHEST CAVITY
920c	11	Yes	Couple c.c. of serous fluid	875c	6	No	Few c.c. of bloody fluid
925c	14	Yes	Couple c.c. of serous fluid	883c	11	No	20 c.c. of bloody fluid
974c	7	No	Couple c.c. of serous fluid	20d	37	No	Few c.c. of serous fluid
978c	55	Yes	Couple c.c. of serous fluid	23d	32	No	Few c.c. of bloody fluid
994c	44	No	Couple c.c. of serous fluid	44d	25	No	25 c.c. of bloody fluid
959c	37	No	Couple c.c. of serous fluid	54d	21	No	Few c.c. of bloody fluid
33d	27	Yes	Couple c.c. of serous fluid	57d*	18	No	Few c.c. of serous fluid
				91d	21	No	Few c.c. of bloody fluid

*Developed pleurocutaneous fistula which closed on the tenth postoperative day.

RESULTS

The results are summarized in Tables I, II, and III. At autopsy in each animal the mediastinum was found shifted to the right side and the diaphragm on the same side was elevated. Of the 7 control animals in Group A (which did not receive heparin), 4 developed adhesions and 3 did not. A few cubic centimeters of serous fluid was found in the chest cavity in each instance.

TABLE II. PNEUMONECTOMY AND PLEURECTOMY

NONHEPARINIZED GROUP				HEPARINIZED GROUP			
DOG NO.	SURVIVAL (DAYS)	ADHESIONS IN CHEST CAVITY	OTHER CONTENTS IN THE CHEST CAVITY	DOG NO.	SURVIVAL (DAYS)	ADHESIONS IN CHEST CAVITY	OTHER CONTENTS OF THE CHEST CAVITY
196d	5	Yes	Bloody pus	205d	5	No	Few c.c. of bloody fluid
202d	34	Yes	Few c.c. of serous fluid	226d	27	No	Few c.c. of serous fluid
230d	26	Yes	Few c.c. of serous fluid	231d	26	No	Few c.c. of serous fluid
242d	4	Yes	Few c.c. of bloody fluid	243d*	24	No	Few c.c. of serous fluid
309d	6	Yes	Few c.c. of serous fluid	302d	5	No	20 c.c. of bloody fluid

*It had developed pleurocutaneous fistula which closed within 16 days.

All of the control dogs in Groups B and C which did not receive heparin developed adhesions, and the hemithorax contained from a few cubic centimeters to as much as 50 c.c. of either serosanguineous fluid or bloody pus.

All animals in Groups A, B, and C which received sodium heparin were found at autopsy to be free of adhesions and loculations, and, in the chest cavity of each, was found from a few to 50 c.c. of serosanguineous fluid.

At autopsy, cultures of the fluid from the chest cavity grew from each animal in which the chest cavity had been contaminated with coagulase-positive staphylococcus the same organism, except in the case of those which had received Chloromycetin; in one instance the culture was sterile, and the other grew out a Proteus. Among the animals whose chest cavity had been contaminated with pneumococci, cultures of one grew the same bacteria, another grew staphylococcus, coagulase negative, and the remaining two grew staphylococcus, coagulase negative, with beta hemolytic streptococcus.

COMMENT

Eighteen years after the first description by Howell[2] of the discovery of heparin and one year after the first clinical application of heparin, Widstrom and Wilander[3] used heparin in the experimental treatment of induced pleurisy in rabbits. They found that animals which received heparin intrapleurally in doses above 10 mg. daily for 2 days showed no adhesions of fibrin coating of the lung, although each control animal showed a marked amount of fibrin coating and adhesions. No subsequent work regarding the effects of intrapleural injection of heparin could be found in our review of the literature.

TABLE III. PNEUMONECTOMY, PLEURECTOMY, AND CONTAMINATION OF THE PLEURAL SPACE

NONHEPARINIZED GROUP								HEPARINIZED GROUP							
DOG NO.	TYPE OF BACTERIA USED	AMOUNT OF BACTERIA GIVEN	ANTIBIOTIC	SURVIVAL (DAYS)	ADHESIONS IN CHEST CAVITY	CULTURE OF CHEST CAVITY	OTHER CONTENTS OF CHEST CAVITY	DOG NO.	TYPE OF BACTERIA USED	AMOUNT OF BACTERIA GIVEN	ANTIBIOTIC	SURVIVAL (DAYS)	ADHESIONS IN CHEST CAVITY	CULTURE OF CHEST CAVITY	OTHER CONTENTS OF CHEST CAVITY
954c	Staph.	0.5 c.c.	Chloromycetin	9	Yes	−*	25 c.c. bloody fluid	969c	Staph.	0.5 c.c.	Chloromycetin	15	No	−	Few c.c. serous fluid
153d	Staph.	0.5 c.c.	Penicillin and streptomycin	11	Yes	+	15 c.c. bloody pus	2690	Staph.	0.5 c.c.	Penicillin and streptomycin	14	No	+	50 c.c. bloody fluid
268d	Staph.	0.5 c.c.	Penicillin and streptomycin	15	Yes	+	Few c.c. bloody pus	240d	Staph.	0.5 c.c.	Penicillin and streptomycin	8	No	+	Few c.c. bloody fluid
271d	Staph.	0.5 c.c.	Penicillin and streptomycin	14	Yes	+	Few c.c. of pus	114d	Staph.	0.5 c.c.	No	6	No	+	Few c.c. bloody fluid
995c	Staph.	0.5 c.c.	No	6	Yes	+	20 c.c. of bloody fluid	325d	Pneum.	1 c.c.	No	5	No	−***	Few c.c. bloody fluid
327d	Pneum.	1 c.c.	No	5	Yes	−**	Few c.c. serous fluid	347d	Pneum.	1 c.c.	No	7	No	+	30 c.c. bloody fluid
353d	Pneum.	1 c.c.	No	5	Yes	−***	Few c.c. serous fluid								

*Grew Proteus; no staphylococcus.
**Grew staphylococcus, coagulase negative.
***Grew staphylococcus, coagulase negative, and beta hemolytic streptococcus.

Four years later, in 1940, Lehman[4] described his experience in prevention of peritoneal adhesions with intraperitoneal injection of heparin. He demonstrated that the re-formation rate of adhesions after the intraperitoneal administration of heparin in animals was approximately 30 per cent while the average re-formation rate in controls was 147 per cent.

In their experimental studies, Widstrom and Wilander started the administration of herapin immediately after the onset of induced pleurisy and Lehman started the introduction of heparin immediately after the division of intraperitoneal adhesions. Our experiment differed in that injection of intrapleural heparin was started 24 hours after pneumonectomy, so timed to permit transitory postoperative oozing from the chest wall to cease.

There are two theoretical explanations for the effect of heparin in the prevention of organization of exudate and formation of adhesions in the present experiments. First, that which was originally proposed by Lehman that heparin diminishes the coagulability of the initial serous exudate which is later absorbed slowly. Second, that the fibrin formed during the first 24 hours after operation (while no heparin was given) is lysed by a fibrinolytic system which is activated by the presence of heparin as was shown in vitro by von Halse.[5] Von Halse speculated that such fibrinolytic activity takes place as a result of an enzyme, profibrinolysin, subsequently activated by heparin to fibrinolysin which produces lysis of the formed coagulum.

Perhaps as a result of either or both of these two possible actions of heparin, the contents of the chest cavity after pneumonectomy are maintained in a fluid state and, with absorption, a clean pleural space results.

In conclusion, this study indicates that heparin given intrapleurally prevents the formation of adhesions in the presence or absence of infection, and might be of clinical use in the prevention of organization of exudate and multiloculation of fluid in the chest cavity when this seems desirable.

SUMMARY

1. The effect of intrapleural injection of sodium heparin was studied in three groups of experimental animals with appropriate controls: (1) pneumonectomy, (2) pneumonectomy and pleurectomy, and (3) pneumonectomy, pleurectomy, and bacterial contamination of the pleural space.

2. Under the conditions of these experiments the study indicates that the administration of heparin intrapleurally prevents the organization of exudate and the formation of adhesions in the chest cavity.

3. The possible explanations for the prevention of post-pneumonectomy pleural adhesions and multiloculation by the intrapleural injection of heparin are discussed.

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EXPERIMENTAL USE OF SYNTHETIC MESH FOR SUPPORT OF ESOPHAGEAL ANASTOMOSES

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THE greater hazard of esophageal anastomoses in comparison with those carried out between segments of the gastrointestinal tract is well known. The absence of a serosal covering and the essentially longitudinal nature of the esophageal musculature are factors which contribute to the the greater risk of anastomotic disruption. The tensions which might lead to an anastomotic disruption are concentrated upon a relatively tenuous suture line. By distributing the potential tensions along a length of esophagus on both sides of the anastomosis through the use of a supporting mesh secured to the esophagus, it is possible that some increase in suture line stability might be achieved. The availability of biologically inert plastics makes possible the use of meshes constructed from these materials in the support of esophageal anastomoses. The purpose of this study was to investigate the suitability of cylinders and strips of nylon and Teflon mesh for the support of relatively tenuous esophageal anastomoses in dogs.

MATERIAL AND METHODS

Healthy mongrel dogs were used. The weight of the dogs ranged from 8 to 14 kilograms. Intravenous Pentothal sodium was utilized for anesthesia. Oxygen was administered through an endotracheal tube by means of a mechanical respirator. A left thoracotomy was carried out through an intercostal space incision.

The lower third of the esophagus was mobilized and the vagus nerves were dissected away from the esophagus. The upper and lower portions of the mobilized esophagus were occluded by Potts coarctation clamps. The esophagus was transected between the clamps. On occasion, a short segment of esophagus was resected. An end-to-end anastomosis was carried out between the ends of the divided esophagus. A standard, less than careful, esophageal anastomosis was performed. Four interrupted sutures of 4-0 silk were used to approximate esophageal mucosa at the 4 quadrants of the open ends of esophagus (Fig. 1). It should be noted that the esophageal mucosa of the dog is somewhat tougher than that of man. The anastomosis was completed by approximating the esophageal muscle layer by means of a continuous, over-and-over suture of 6-0 arterial silk.

The anastomoses were supported by a fine mesh of nylon or a more coarse mesh of Teflon of the Harrison type. The mesh was attached to the esophagus above and below the anastomosis by a series of diffusely scattered interrupted sutures of 5-0 arterial silk

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which included both the mesh and the esophageal musculature. Both cylinders and strips of mesh were employed. The cylinders were constructed by wrapping a sheet of mesh around the esophagus in the area of the anastomosis and overlapping slightly the ends of the sheet. Strips of mesh were attached to the esophagus above and below the anastomosis in an interrupted manner to act as struts across the anastomosis. The strips were investigated in order to find a means of support which might be more applicable to the problem of reinforcing esophageal anastomoses carried out in the growing infant or child. It was believed that the encircling cylinder type of support would not be suitable for use in this age group.

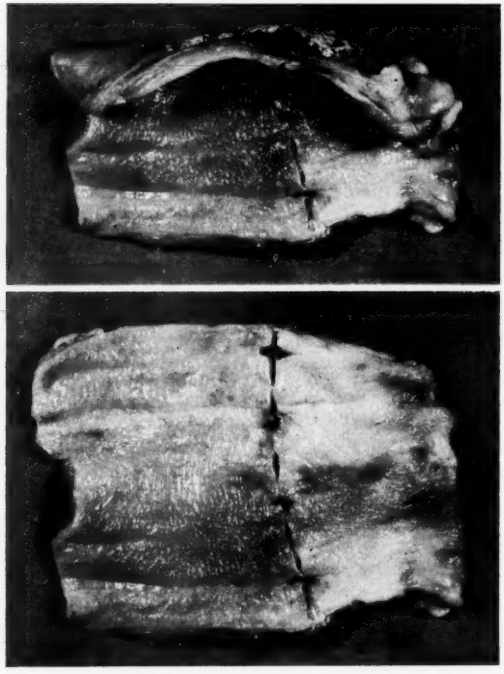

Fig. 1.—Photographs illustrating the nature of the esophageal anastomosis and support as it appeared in the early postoperative period on autopsy 7 days after operation (Dog 303).

At the completion of the anastomosis and the placement of the supporting mesh, the occluding Potts coarctation clamps were released and the esophagus was returned to its normal anatomic position. A small amount of penicillin-streptomycin mixture was left in the chest in the area of the anastomosis. The thoracotomy incision was closed in layers and a catheter which was left in the chest during the closure was aspirated and withdrawn.

RESULTS

Cylinders or strips of synthetic mesh, nylon or Teflon, were used to support relatively weak esophageal anastomoses in 18 dogs. Nylon cylinders were employed in 2 animals, Teflon cylinders in 7, and Teflon strips in 9 (Table I).

The integrity of the anastomosis and the suitability of the synthetic mesh support were investigated at postmortem examination from 4 to 365 days

after operation. Four animals died from 4 to 68 days after operation and 14 were sacrificed from 5 to 365 days after operation. None of the deaths was due to anastomotic leakage or disruption. Neither empyema nor local abscess formation was found at autopsy in any of the animals. The synthetic mesh support appeared on gross and microscopic examination to be well tolerated and had remained in place in all. There was no evidence of infection or inflammation about the mesh in any animal on gross examination of the external appearance of the esophagus. Examination of the opened lumen of the esophagus revealed excellent healing and epithelization of the esophageal

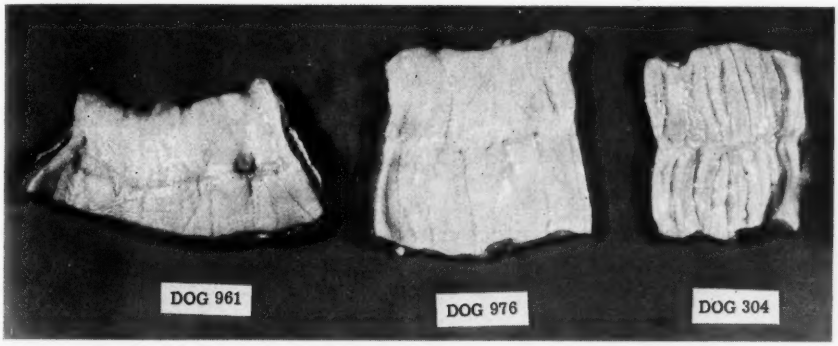

Fig. 2.—Photographs showing the appearance of the mucosal surface of 3 supported esophageal anastomoses. Except for a small granuloma in Dog 961, the areas of anastomosis are well healed and epithelized. There is dilatation of the proximal esophageal segment (*lower*) of the Teflon cylinder supported anastomosis in Dog 961, but none in Dogs 976 and 304 in which Teflon strips were employed. The interval from operation to autopsy in these animals ranged from 107 to 142 days.

TABLE I. SUMMARY OF EXPERIENCE WITH THE USE OF SYNTHETIC MESH FOR THE SUPPORT OF ESOPHAGEAL ANASTOMOSES

DOG	TYPE OF SYNTHETIC MESH SUPPORT FOR ANASTOMOSIS	INTERVAL, OPERATION TO AUTOPSY (DAYS)	ANASTOMOTIC DISRUPTION OR LEAKAGE	INFECTION IN AREA OF MESH	POSITION OF MESH INTACT AT AUTOPSY	TISSUE REACTION TO MESH	ESOPHAGEAL DILATATION PROXIMAL TO MESH
872	Nylon cylinder	40	None	None	Yes	Minimal	Yes
873	Nylon cylinder	90	None	None	Yes	Minimal	Yes
960	Teflon cylinder	4	None	None	Yes	Minimal	No
912	Teflon cylinder	68	None	None	Yes	Minimal	No
317	Teflon cylinder	99	None	None	Yes	Minimal	Yes
997	Teflon cylinder	113	None	None	Yes	Minimal	Yes
990	Teflon cylinder	124	None	None	Yes	Minimal	Yes
969	Teflon cylinder	136	None	None*	Yes	Minimal	Yes
961	Teflon cylinder	142	None	None*	Yes	Minimal	Yes
366	Teflon strips	5	None	None	Yes	Minimal	No
303	Teflon strips	7	None	None	Yes	Minimal	No
967	Teflon strips	55	None	None	Yes	Minimal	No
331	Teflon strips	92	None	None	Yes	Minimal	No
330	Teflon strips	98	None	None	Yes	Minimal	No
304	Teflon strips	107	None	None	Yes	Minimal	No
1000	Teflon strips	117	None	None	Yes	Minimal	No
976	Teflon strips	128	None	None	Yes	Minimal	No
975	Teflon strips	365	None	None	Yes	Minimal	No

*Single small granuloma on mucosal surface in area of anastomosis.

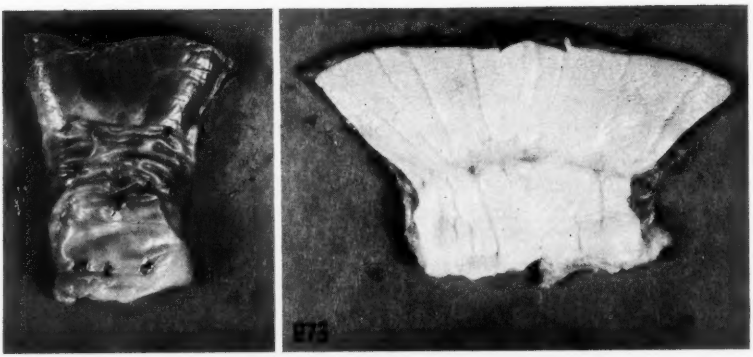

Fig. 3.—Photographs of area of nylon cylinder supported esophageal anastomosis before and after opening the esophagus of Dog 873, 90 days after operation. Significant dilatation of the proximal esophageal segment (*upper*) is shown. There is some wrinkling of the fine mesh nylon.

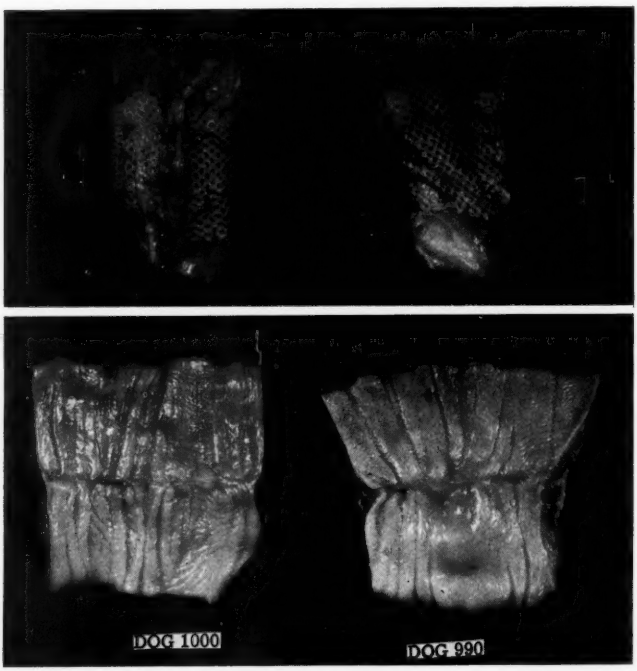

Fig. 4.—Photographs showing the appearance of the Teflon strip supported esophageal anastomosis before and after opening 117 days after operation in Dog 1,000, and of the Teflon cylinder supported anastomosis in Dog 990 after 124 days.

mucosa in all but the 3 animals studied from 3 to 7 days after operation (Fig. 2). This satisfactory mucosal healing was observed despite the rather loose mucosal approximation at operation with the use of only 4 interrupted mucosal sutures. A rather small suture line granuloma was found on inspection of the lumen of the esophagus in 2 animals (Dogs 961 and 969). A small piece of silk was observed at the base of the granuloma in 1 animal.

A cylinder made of fine mesh nylon was employed for esophageal anastomotic support in 2 animals. Although the mesh was tolerated well, some wrinkling of the mesh was found at postmortem examination. The most significant gross finding was the occurrence of rather marked esophageal dilatation proximal to the anastomosis (Fig. 3). This finding suggested the production of some esophageal obstruction at the site of the circumferential mesh support. One of the animals died of malnutrition 40 days after operation. The proximal esophageal dilatation in these 2 animals was greater in degree than that observed when cylinders of wider mesh Teflon were used.

Cylinders made of wide mesh Teflon were used for anastomotic support in 7 animals. The mesh was tolerated well and wrinkling did not occur. Significant dilatation of the esophagus proximal to the anastomosis occurred in all but 2 animals. One of these animals was studied at autopsy only 4 days after operation and the other 1 was the only animal in this group in which overlapping of the mesh had not been produced in the creation of the cylinder. Hence, in this animal, no complete, potentially constricting, or limiting ring had been produced.

Interrupted strips of wide mesh Teflon were used for support across the anastomosis in 9 animals. All were tolerated well and retained their position without wrinkling or distortion. Dilatation of the esophagus proximal to the anastomosis did not occur in any of the animals (Fig. 4).

DISCUSSION

The suitability of oval patches of fine mesh nylon for the replacement of resected areas of esophageal musculature was reported in 1959 by the senior author and Bounous.[1] The mucosa was not opened in these animals and there was no problem of potential infection or disruption as encountered in esophageal anastomoses.

In the present study, the feasibility of employing synthetic mesh for the support of esophageal anastomoses was investigated. Fine mesh nylon and wide mesh Teflon were employed as cylinders or strips and were secured to the wall of the esophagus above and below the anastomosis with a series of interrupted sutures of fine silk. A purposely non-careful end-to-end esophageal anastomosis had been carried out.

In all of 18 animals the mesh supports were tolerated well on gross and microscopic examination from 4 to 365 days after operation. There was no evidence of anastomotic leakage or disruption and no evidence of localized or general infection. All of the mesh supports remained in position without distortion. Some wrinkling of the fine mesh nylon cylinders did occur.

The use of cylinders with circumferential support was found to be uniformly unsatisfactory due to the production of esophageal dilatation proximal to the anastomosis. The esophageal dilatation was most marked when fine mesh nylon cylinders were employed. Dilatation of the proximal esophageal segment did not occur when interrupted strips of Teflon mesh were used.

It is possible that the optimum size of mesh may be between the rather fine mesh of the nylon used in this study and the wide mesh of the Teflon employed. It also is probable that Teflon mesh may prove to be the most suitable.

The results of this study suggest that interrupted strips of Teflon mesh may prove to be of value in the support of potentially weak esophageal anastomoses when indicated.

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A METHOD OF LONG-TERM CARDIAC ACTIVATION

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PERCUTANEOUS activation of the heart in A-V dissociation by a pacemaker is attended by infection of the activation electrode and concomitant rise in activation voltage. A method to obviate these difficulties is described.

METHOD

Mongrel dogs were anesthetized with intravenous Pentothal sodium and endotracheal intubation performed. Respirations were maintained by a Starling respirator. Preoperative normal electrocardiograms were taken (Fig. 1). A standard right thoracotomy was then done and the chest entered in either the fifth or sixth intercostal space. After the superior and inferior venae cavae were freed and isolated, total inflow occlusion of the right heart was performed and a right auriculotomy made. The atrioventricular node was identified and destroyed (Fig. 2). The ensuing complete heart block is demonstrated (Fig. 3).

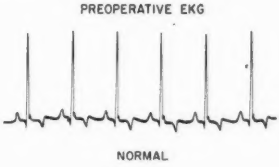

Fig. 1.

Pacemaker activation electrodes were then placed in the myocardium and chest closure with underwater seal drainage completed. The response to pacemaker activation is shown (Fig. 4), demonstrating that each QRS complex is immediately preceded by a pacemaker impulse.

The three ways in which the activator was connected are: (1) an insulated wire (except the tip) was anchored in the myocardium and brought out through the chest wall and skin, (2) an insulated wire anchored in the myocardium and connected to an uncovered grid implanted in the subcutaneous tissue and, (3) an insulated wire anchored in the myocardium and brought out to a covered grid implanted in the subcutaneous tissue (Fig. 5).

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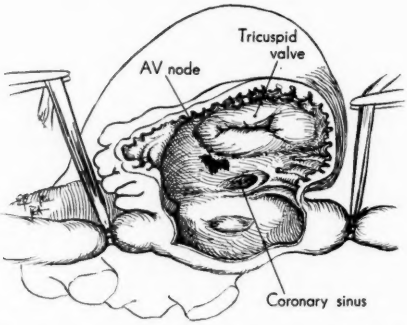


Fig. 2.—Right atrium exposure of an A-V node.

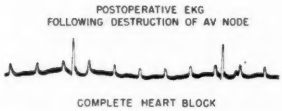
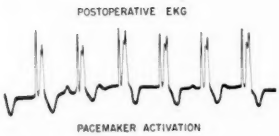


Fig. 3.



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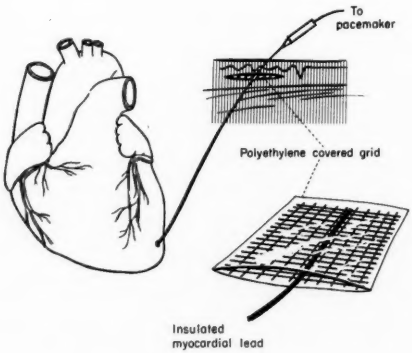

Fig. 5.

RESULTS

In the single insulated wire, a chronic inflammation developed at the site of exit through the skin associated with a rising activation potential of the pacemaker (Fig. 6).

When a grid is buried in the subcutaneous tissue, it is well tolerated and does not become infected. However, because of the fibrotic process at the site of implantation, the voltage required to activate the heart increases (Fig. 7).

When the subcutaneous grid is covered with polyethylene, the grid neither becomes infected nor is there any rise in activation voltage (Fig. 8). The grid has been functional for as long as 6 weeks.

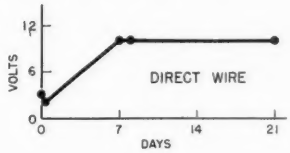

Fig. 6.

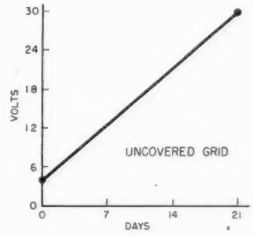

Fig. 7.

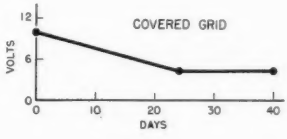

Fig. 8.

SUMMARY

1. A surgical technique for experimentally producing a permanent complete heart block is described.

2. A practical method of imbedding a pacemaker electrode is described.

3. In a protected electrode there is neither infection nor a rise in activation potential.

4. Activation has been intermittent to date. Efficacy when used continuously has not been determined.

VULNERABILITY OF THE DOG HEART TO VENTRICULAR FIBRILLATION: A COMPARATIVE STUDY OF CHRONIC ISCHEMIA AND THREE MYOCARDIAL REVASCULARIZATION PROCEDURES

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VENTRICULAR fibrillation, almost without exception, is the cause of death after coronary occlusion in the dog. The incidence of ventricular fibrillation as the mechanism of death after coronary occlusion in the human being is more difficult to ascertain but is believed by many to be common.[3, 10] Several clinicopathologic investigations support this concept.[2, 19]

The present study was undertaken to quantitate, by means of threshold measurements, the vulnerability of the dog heart to ventricular fibrillation after chronic myocardial ischemia and after the performance of three operative procedures designed to revascularize the heart. It was dissatisfaction with mortality studies after coronary occlusion that led to the use of the threshold technique. In a well-controlled experiment by Chardack and co-workers,[5] the conclusion was reached that mortality studies made after experimental coronary ligation are an unsatisfactory tool for analysis of possible benefits derived from surgical procedures designed to protect the dog from such ligation. Burchell,[4] in 1940, after a survey of the literature on this problem, concluded that the mortality following coronary occlusion varied from 0 to 100 per cent.

The replacement of inexact bioassay techniques by the use of modern electronic instrumentation combined with threshold measurements, as first suggested[17] and later applied[16, 18] by Wiggers, affords one the opportunity to measure the degree of change a given factor has induced and to do this under controlled conditions. Previous investigation[11] suggested that implantation of the internal mammary artery into the myocardium of the left ventricle, as devised by Vineberg,[15] offered considerable protection from ventricular fibrillation if the implanted vessel remained patent. The present study compares the results obtained with poudrage and coronary sinus narrowing (Beck[1] operation) and pulmonary artery to left atrial shunt (Day and Lillehei[7]) with the Vineberg operation and with chronic ischemia alone.

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*Markle Scholar in Medical Sciences.

METHODS

This investigation was performed on adult mongrel dogs of either sex, weighing between 12.5 and 20.0 kilograms. Following intravenous pentobarbital anesthesia, 30 mg. per kilogram, the animals were intubated with an endotracheal tube and ventilated with compressed room air using an electronic respirator. Additional anesthesia was given in small increments of 25 to 50 mg. intravenously. The minor alterations in depth of anesthesia that occurred throughout these experiments has been shown not to alter significantly the fibrillation threshold.[12] The esophageal temperature was measured and was maintained at between 37.5° and 38.5° C., utilizing a Hypo-Hyper Thermia unit.* Previous studies have indicated that esophageal temperature most closely reflects cardiac temperature and is superior to the rectal temperature.[12]

Sterile technique was used for all procedures. The heart was exposed through a left thoracotomy in the fifth intercostal space. The pericardium was incised longitudinally and all thresholds were determined on the left ventricle in the area of distribution of the anterior descending branch of the left coronary artery.

The instrumentation used was similar to that described by Shumway, Johnson, and Stish.[14] Amplified electrocardiogram potentials were fed into a triggering circuit, the output of which was coupled to the synchronizing input of a Grass stimulator.† The output of the stimulator was connected to a bipolar electrode. One lead of the electrode contained a 2,500 ohm resistor to minimize the effects of changing resistances between the electrodes and the cardiac surface. Two oscilloscopes were used. On one the electrocardiogram was displayed. The stimulator output was applied to this oscilloscope so that brightening of the trace at the moment of stimulation provided a direct method of determining precisely the location of the stimulus in the cardiac cycle. The other oscilloscope was used to determine the magnitude in milliamperes of the current delivered. The trigger circuit provided a single synchronizing pulse for the stimulator upon the occurrence of the first R wave after the trigger button was released. A wide range of stimulus strength, duration, and delay were provided by the stimulator. A stimulus duration of 10 msec. was used in all testing. In all animals studied, an initial ventricular fibrillation threshold was determined by sweeping the vulnerable period (terminal 30-90 msec. of systole) of the cardiac cycle with stimuli of increasing current strength from subthreshold to threshold levels. The criterion of threshold was persistent ventricular fibrillation.

The delay setting of the stimulator, which could be varied, was helpful in accurately sweeping the cardiac cycle. The delay period, which determined precisely the location in the cardiac cycle when the stimulus was delivered, was measured from the R wave in the QRS complex. A single stimulus of 10 msec. duration was delivered to the heart beginning shortly after the QRS com-

*Therm-O-Rite Products Corporation, 1748 Main St., Buffalo, N. Y.
†Grass Model S4 Stimulator, Grass Instrument Co., 101 Old Colony Ave., Quincy, Mass.

plex and was repeated in subsequent cardiac cycles throughout the vulnerable period, and beyond, by progressively increasing the delay in time from the R wave, 5 msec. after each stimulus.

Since the duration of stimulus was 10 msec. and the delay from the R wave was increased with 5 msec. increments, we could deliver stimuli to the heart, before, during, and after the entire vulnerable period. After sweeping the entire vulnerable period at one subthreshold strength, the procedure was repeated after increasing the current strength by from 1.0 to 1.5 Ma. This was repeated until ventricular fibrillation was produced at which time the location on the heart surface and the strength of stimulus were recorded.

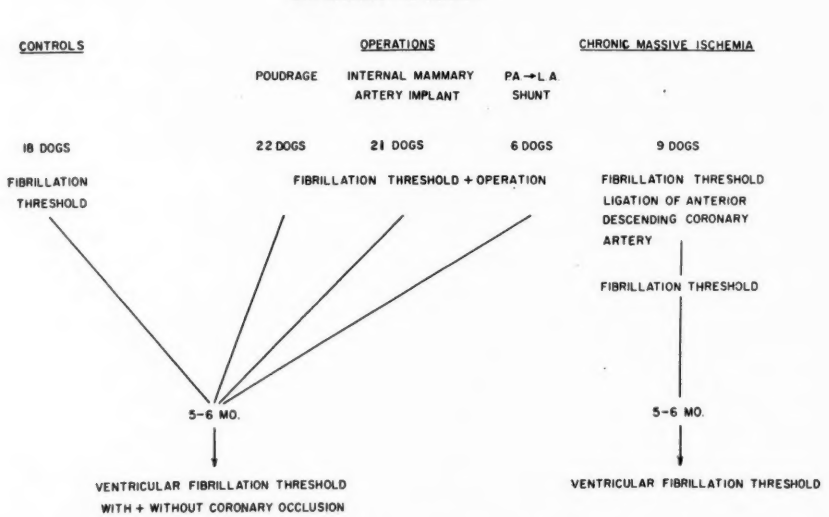

Fig. 1.—The experimental design is illustrated for the present study. Three groups of dogs were studied: Controls, Operative Group, and Chronic Massive Ischemia Group. Further explanation appears in the text.

The instrumentation provided a single square wave stimulus of known strength, and known duration which could be delivered at a known, measurable and alterable time in the cardiac cycle and which was applied to a known area on the heart surface.

After accomplishing fibrillation, the heart was defibrillated quickly, usually in less than 10 seconds, using standard equipment.

The determination of ventricular fibrillation thresholds by the method outlined was made initially and after 6 months on the following groups of animals (Fig. 1).

1. *Controls.*—18 dogs.

2. *Operative Group.*—(a) Animals in which the left internal mammary artery was implanted into the left ventricle after the method of Vineberg[15]—22 dogs. (b) Animals in which a cardiac poudrage was performed as described

by Beck[1]—22 dogs. (c) Animals in which a pulmonary artery-left atrial shunt had been performed as suggested by Day and Lillehei[7]—6 dogs.

3. *Chronic Ischemia Group.*—Animals in which the left anterior descending coronary artery was ligated at the time of the original operation—9 dogs.

Initially the fibrillation threshold was determined without coronary occlusion and with temporary coronary occlusion (left anterior descending) in all groups. The animals were then either closed (controls), subjected to a surgical procedure (operative group), or the anterior descending artery was permanently ligated (chronic ischemia group). After 5 to 6 months the animals were reoperated upon and, using the same technique, the fibrillation threshold was redetermined with and without coronary occlusion in the control and operative groups. In the animals with permanent ligation of the anterior descending coronary artery (chronic ischemia) the threshold was determined without additional ligation.

Five animals shown to have "protection" from the internal mammary artery implantation after the left anterior descending artery was occluded underwent a further determination of the ventricular fibrillation threshold with occlusion of the implanted internal mammary artery also.

Determination of patency of the internal mammary artery implants was made either on the basis of plastic injection of the vessels or on histologic sections.

RESULTS

The results appear in Table I and Figs. 2 and 3. An "analysis of variance"[13] was completed for the treatment groups. This compared the variability among treatment groups with the variability within treatment groups.

TABLE I. VENTRICULAR FIBRILLATION THRESHOLD BEFORE, IMMEDIATELY AFTER, AND 6 MONTHS AFTER LAD* CORONARY ARTERY LIGATION

DOG NUMBER	INITIAL THRESHOLD		THRESHOLD AFTER 6 MO.
	WITHOUT CORONARY OCCLUSION (Ma.)	WITH CORONARY OCCLUSION (Ma.)	
1725	22.5	—	7.5
1876	22.5	1.5	7.5
1877	17.5	4.5	13.0
1881	16.0	8.0	8.0
1890	18.5	8.0	12.5
1897	14.0	6.0	7.5
1917	17.5	5.5	7.5
1919	18.5	7.0	—
1910	20.0	5.0	4.5
Mean	18.5	5.7	8.5

*LAD—Main left anterior descending coronary artery. Septal artery was not ligated in any animals reported.

The effect of internal mammary artery implantation when this artery remained patent was to prevent the marked drop in the ventricular fibrillation threshold after coronary occlusion. This effect was significant at the 1 per cent level. If the internal mammary artery was demonstrated to be thrombosed,

the marked drop in fibrillation threshold after coronary occlusion was not prevented. No significant difference existed between the decline seen in the animals with internal mammary implantation, when this vessel had thrombosed, and that seen in the control group.

Five animals with open internal mammary artery implants, which afforded excellent "protection" with the left anterior descending coronary artery occluded, showed a marked drop in the fibrillation threshold after the implanted internal mammary artery was occluded (Fig. 3).

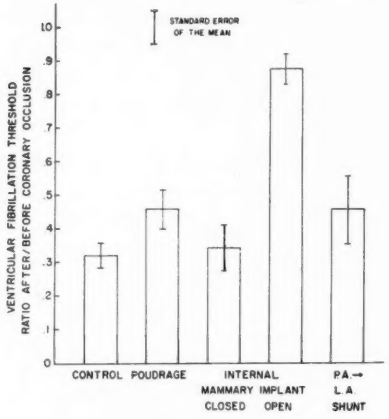

Fig. 2.

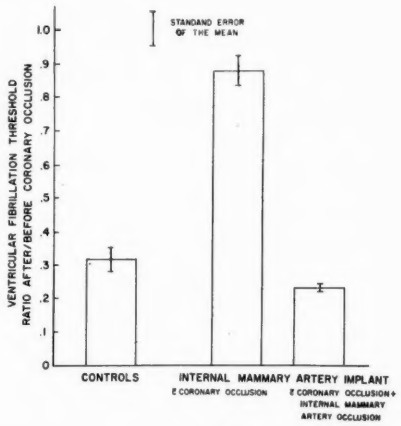

Fig. 3.

Fig. 2.—The results are illustrated for control and operative groups of dogs. The ventricular fibrillation threshold after 6 months is expressed as a ratio after/before coronary occlusion. Poudrage, pulmonary artery to left atrial shunt, and internal mammary artery implant (closed) did not vary from controls, indicating no decrease in the vulnerability to ventricular fibrillation as a result of these procedures. In contrast, internal mammary artery implant (open) provided marked protection from ventricular fibrillation associated with coronary occlusion. The threshold in the latter group remained at 88 per cent of normal even with coronary occlusion.

Fig. 3.—Results are illustrated for controls compared to successful Vineberg procedures. There is only a slight drop to 88 per cent of normal when occlusion of the anterior descending coronary artery is induced. When, in addition, the patent internal mammary artery is occluded, the threshold drops markedly to the range seen in controls.

The Beck operation and pulmonary artery to left atrial shunt did not prevent the marked decline in the ventricular fibrillation threshold associated with acute coronary occlusion (Fig. 2). No significant difference from controls existed. The pulmonary artery to left atrial shunt was sufficiently large in each dog to cause peripheral oxygen desaturation below 90 per cent and the period between creation of the shunt and testing was longer than considered by Day[6] to be necessary for the development of intercoronary collateral vessels.

In Table I the results of massive ischemia alone are illustrated. In these animals the ventricular fibrillation threshold had been determined, the left anterior descending coronary artery ligated, and the threshold redetermined. The survivors (one third of the group) were kept for 5 to 6 months and the threshold determined in exactly the same area to see if anastomotic vessels had increased the blood supply sufficiently to affect the susceptibility to ventricu-

lar fibrillation. Initially, the mean threshold in these 9 animals was 18.5 Ma., and with occlusion, 5.7 Ma. (mean). The threshold after 5 to 6 months was elevated slightly to 8.5 Ma. (mean) which was not a significant change for the sample size. This is a selected group of animals but selected in the direction to show greater rather than less collateral circulation if this affects survival favorably.

DISCUSSION

The results of this investigation suggest that a greater resistance to ventricular fibrillation associated with coronary occlusion can be offered by operative means than by ischemia alone. However, the only procedure which decreased the vulnerability of the dog ventricle to fibrillation after coronary occlusion was the Vineberg operation and this procedure only when the internal mammary artery remained patent. Neither poudrage (Beck operation), nor pulmonary artery to left atrial shunt, nor previous thoracotomy and pericardiotomy resulted in any significant elevation of the fibrillation threshold over controls.

This technique is recommended for this purpose over mortality studies after coronary occlusion which have a wide range even when performed at the same anatomic site by the same operator in the same laboratory. Since ventricular fibrillation is the predominant cause of death in the experimental animal (dog) after coronary occlusion, measurement of the fibrillation threshold is a logical determination to assess factors believed to influence coronary occlusion favorably or not.

While intercoronary collaterals undoubtedly develop as the result of ischemia and the operations performed, the measure of function assessed by the present study would suggest that the actual blood flow is inadequate. Reduction in mortality or the demonstration of collateral vessels by plastic injection techniques does not necessarily indicate a significantly improved coronary circulation. To establish the latter it would be necessary to show that a sufficient quantity of blood entering the coronary sinus had actually traversed the capillary bed of the left heart. As Gregg[8] states, there is no adequate method available to quantitate the extent of development of the collateral coronary bed as a result of acute or chronic coronary occlusion.

There seems to be little doubt that survival after coronary occlusion and decreased vulnerability to ventricular fibrillation are related directly to blood supply to the relatively ischemic area of myocardium. There is a great need for a direct measurement of "tissue blood flow" or that component of the blood supply to an organ which actually serves in the nutrition of the tissue. If one could quantitate the minimal tissue needs in terms of milliliters of blood per gram per minute and measure that supplied after various operations or after the influence of physiologic, physical, and chemical factors, much of the present confusion and indecision would be eliminated. The use of deuterium oxide as a tracer substance to measure tissue blood flow, as described by Johnson, Cavert, and Lifson,[9] may be the ultimate solution to this problem.

SUMMARY

The vulnerability of the dog heart to ventricular fibrillation after coronary occlusion and the influence of three myocardial revascularization procedures and chronic ischemia have been quantitatively assessed by the measurement of ventricular fibrillation thresholds.

Acute ligation of the anterior descending branch of the left coronary artery causes an immediate drop in the fibrillation threshold to approximately one fourth to one third of normal. This is not changed if one releases the artery and re-tests the animal with occlusion 5 to 6 months later, indicating no effect from thoracotomy and pericardiotomy alone.

The three operative procedures designed to revascularize the heart which were tested had a variable effect on the fibrillation threshold. Poudrage and pulmonary artery to left atrial shunt did not increase the resistance of the dog's heart to ventricular fibrillation after coronary occlusion. In contrast, implantation of the internal mammary artery into the myocardium of the left ventricle did decrease the vulnerability to ventricular fibrillation after coronary occlusion. In animals in which the internal mammary artery remained patent, the fibrillation threshold remained after coronary occlusion at 88 per cent (mean) of control without coronary occlusion. This difference is highly significant. If the internal mammary artery was thrombosed, this protection did not exist and no difference from controls was manifest.

That blood supply plays an important role in protection from ventricular fibrillation is suggested not only by the above but by the fact that when the internal mammary artery was patent and it was ligated, in addition, to the coronary artery the threshold dropped to very low levels.

When the anterior descending branch of the left coronary artery was permanently ligated, the expected decline of fibrillation threshold occurred. When the survivors from this group were re-tested 5 to 6 months later the fibrillation threshold had increased slightly but this increase was not statistically significant for the sample size.

The results of this investigation suggest that a greater resistance to ventricular fibrillation associated with coronary occlusion can be achieved with internal mammary artery implantation if that vessel remains patent than by means of pulmonary artery to left atrial shunt, cardiac poudrage, or that which might occur naturally with chronic ischemia alone.

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THE PATCH TECHNIQUE AS AN ADJUNCT TO CORONARY ENDARTERECTOMY

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THE feasibility of coronary endarterectomy in some patients with segmental occlusive disease has recently been demonstrated by Longmire[2] and Bailey.[1, 6] Success of this procedure, however, depends upon proper selection of patients with localized segmental occlusions and the perfection of techniques of small vessel surgery. Recent development of improved methods of coronary arteriography, including cine-roentgenography, have made possible the localization of segmental occlusions with reasonable accuracy, thus facilitating the selection of patients for operation.[5, 9, 10] Once the diagnostic problems have been solved, the need for better techniques of arterial disobliteration and reconstruction will become increasingly important.[4, 7, 8] At present, thrombosis of the vessels after thromboendarterectomy is the principal cause for both early and late failures. In a recent study relating to small vessel surgery we demonstrated that stenosis of the lumen after closure of an arteriotomy was a common cause of thrombosis.[3] To avoid this complication, a technique was described wherein an oval-shaped patch of suitable material was sutured to the wound edges, preventing luminal constriction. This method was successfully applied to coronary and femoral vessels in experimental animals. The following study consists of a more intensive investigation of the application of this technique to coronary artery surgery. A comparison of various types of patch materials was made in experimental animals, and the feasibility of the clinical application of this method was evaluated in human hearts removed at autopsy in which segmental coronary occlusions were present.

METHODS

This investigation was divided into two phases, an experimental study for comparison of the various patch materials in animals and an autopsy study to evaluate the clinical application of the patch technique to human coronary disease.

Animal Experiments.—Patches of various materials including venous autograft, arterial autograft, pericardial sac, and Dacron fabric were compared.

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Arterial and venous autografts were taken from the femoral vessels immediately prior to surgery. The pericardial patches were obtained at the time of the coronary surgery, and the Dacron was cut from a finely knitted crimped arterial prosthesis.

In dogs, weighing 15 to 30 kilograms, the circumflex branch of the left coronary was exposed through a left fourth intercostal space incision (Fig. 1, *a*). After heparinization with 1.5 mg. per kilogram, the vessel was temporarily occluded with rubber bands serving as perivascular tapes. A longitudinal incision, 5 to 10 mm. in length, was made in the vessel and an intraluminal polyethylene shunt was inserted (Fig. 1, *b* and *c*). Immediately prior to completing the suture line the shunt was removed and each end of the vessel

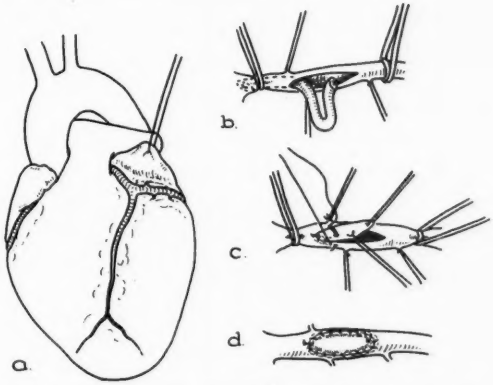

Fig. 1.—Diagram which demonstrates the use of an intraluminal polyethylene shunt to maintain flow during the suturing of a patch on the circumflex branch of the left coronary.

was flushed to assure patency. The suture line was then quickly completed and flow was re-established in the vessel. Polybrene (3 mg. per kilogram) was given to neutralize the heparin. All animals alive 60 days after surgery were sacrificed and the coronary arteries were examined to determine patency.

Autopsy Study.—Radiopaque visualization of the coronary arteries in 100 random hearts removed at autopsy was accomplished by injection of a 40 per cent suspension of barium sulfate solution into the vessels. Over-penetrated roentgenograms were then made in an attempt to demonstrate occlusive disease. When the obstructive process was segmental in nature, a longitudinal incision was made in the vessel and an endarterectomy was performed. The endarterectomy incision was closed with an arterial patch and the barium injections were repeated to determine the results of endarterectomy and to evaluate the patch technique of arteriotomy closure.

RESULTS

Experimental Animal Study.—

Venous autograft: As shown in Table I there were 10 dogs in which a vein graft was employed and, of these, four were patent at the time of death.

TABLE I. VENOUS AUTOGRAFT PATCH*

NUMBER	DOG	DAYS ALIVE	STATUS OF CIRCUMFLEX CORONARY	ASSOCIATED FINDINGS
1	H-65	60†	Patent	Heart worms
2	H-54	4	Occluded	Heart worms
3	H-73	1	Occluded	Heart worms
4	H-83	1	Patent	
5	H-92	1	Occluded	
6	I-17	3	Occluded	
7	I-26	1	Patent	Heart worms
8	I-33	60†	Occluded	Heart worms
9	I-51	1	Patent	
10	I-64	1	Occluded	

*Results of femoral venous autograft patches which were sewn on the circumflex branch of the left coronary artery.
†Sacrificed.

It was noted at operation that the vein graft tended to balloon out, and this may have caused excessive turbulence resulting in clotting. It may also be significant that this was the first series carried out, and the surgical technique probably improved with subsequent experience.

Arterial autograft: The best results were obtained with arterial autografts, the coronary artery being patent at the time of death in 7 out of 10 dogs (Table II). The arterial graft was easier to handle and conformed better to the contour of the coronary artery (Fig. 2). In several instances patency was demonstrated following operation by coronary arteriography (Fig. 3). In 2 of the animals sacrificed 60 days after surgery, the inner surface of the patch was smooth and glistening, resembling the host vessel (Fig. 4).

TABLE II. ARTERIAL AUTOGRAFT PATCH*

NUMBER	DOG	DAYS ALIVE	STATUS OF CIRCUMFLEX CORONARY	ASSOCIATED FINDINGS
1	I-77	1	Occluded	Heart worms
2	J-2	60†	Occluded	
3	J-15	1	Occluded	Heart worms
4	J-19	1	Patent	Heart worms
5	J-47	60†	Patent	
6	J-58	1	Patent	Pneumonia
7	J-75	7	Patent	Hemothorax
8	J-87	1	Patent	
9	K-25	4	Patent	Heart worms
10	P-51	60†	Patent	

*Results of femoral arterial autograft patches which were sewn on the circumflex branch of the left coronary artery.
†Sacrificed.

Pericardial sac: Of the 6 animals in which the pericardial sac was used for a patch, 2 had patent vessels at the time of death (Table III). In one vessel, patent 60 days after surgery, the pericardium grossly resembled intima. Technically the pericardium was difficult to handle and occasionally tore at the suture line.

Dacron patch: The results with Dacron patch were poor, with only 2 out of 10 dogs having a patent vessel at the time of death (Table IV). In 1 animal the vessel was patent after 60 days, indicating the suitability of this material if the complication of thrombosis can be avoided (Fig. 5).

Fig. 2.—Photograph which shows an arterial autograft patch on the circumflex branch of the left coronary.

Fig. 3.

Fig. 4.

Fig. 3.—Coronary arteriogram from Dog J-47 made 60 days after a patch had been sewn on the circumflex branch of the left coronary artery (*arrow*) demonstrating patency of the vessel.

Fig. 4.—Photograph of the arterial autograft patch from Dog J-47 made 60 days after surgery when the animal was sacrificed. Note glistening endothelial surface on the patch grossly indistinguishable from host vessel.

TABLE III. PERICARDIAL SAC PATCH*

NUMBER	DOG	DAYS ALIVE	STATUS OF CIRCUMFLEX CORONARY	ASSOCIATED FINDINGS
1	K-40	60†	Occluded	Heart worms
2	K-71	60†	Patent	
3	K-88	3	Patent	Hemothorax
4	K-96	4	Occluded	Heart worms
5	L-2	1	Occluded	Heart worms
6	L-16	4	Occluded	

*Results of pericardial sac patches which were sewn on the circumflex branch of the left coronary artery.
†Sacrificed.

Fig. 5.—Photograph of a Dacron patch from Dog L-79 made 60 days after surgery when the animal was sacrificed.

TABLE IV. DACRON PATCH*

NUMBER	DOG	DAYS ALIVE	STATUS OF CIRCUMFLEX CORONARY	ASSOCIATED FINDINGS
1	L-79	60†	Patent	
2	L-97	60†	Occluded	Heart worms
3	M-9	1	Occluded	
4	M-13	1	Occluded	Heart worms
5	M-26	1	Occluded	
6	M-99	1	Occluded	Heart worms
7	O-39	7	Occluded	Heart worms
8	O-46	60†	Patent	
9	N-48	60†	Occluded	Heart worms
10	N-67	1	Occluded	Heart worms

*Results of Dacron patches which were sewn on the circumflex branch of the left coronary artery.
†Sacrificed.

Autopsy study: Segmental occlusive disease was demonstrated and endarterectomy attempted in 23 of the autopsy hearts. In many of these an atheromatous plug was removed and the arteriotomy was closed with an arterial patch (Fig. 6). Repeat roentgenograms demonstrated the success of endarterectomy and the lack of narrowing at the site of arteriotomy closure (Fig. 7).

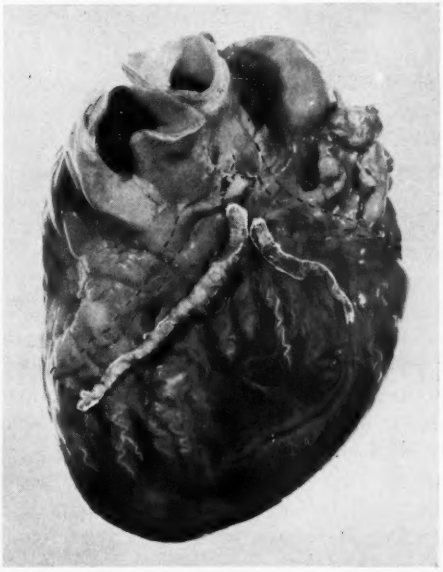

Fig. 6.—Photograph made after endarterectomy of the anterior descending and circumflex branches of the left coronary artery in an autopsy heart which shows the endarterectomized segment placed adjacent to the vessel from which it was removed. Note the arterial patch at the origin of the anterior descending vessel used to widen the arteriotomy site.

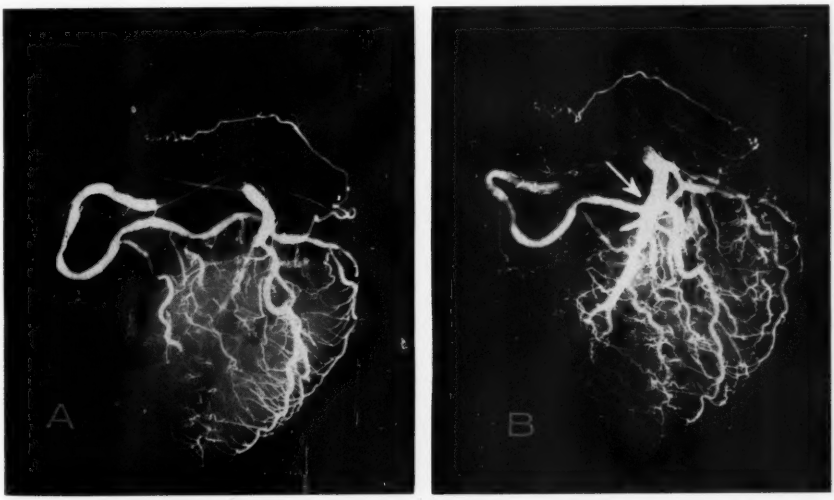

Fig. 7.—Arteriographic studies from an autopsy heart which demonstrate on the left an occlusion of the anterior descending branch of the left coronary. On the right are shown the results of endarterectomy with an arrow indicating the incision site where an arterial patch has been used to widen the vessel.

DISCUSSION

The comparison of various patches is interesting in that at least one long-term patency was obtained with each material. Nevertheless, the incidence of thrombosis varied significantly in the four groups, the best results being obtained with the arterial autograft which remained patent in 7 out of 10 dogs. In the clinical application of this technique, an autograft patch might be conveniently obtained from the internal mammary artery during thoracotomy. The results with the Dacron patch were disappointing since this material has the advantage of availability and ease of handling. It is anticipated, however, that further investigation of other prosthetic materials of a different weave and porosity will result in the development of a suitable fabric for coronary patches. The pericardial sac and venous autograft patches were successful in only a limited number of animals. Furthermore, these materials are both somewhat difficult to handle technically and seem less suitable than arterial autograft.

The over-all results of the animal study may have been adversely affected by the high incidence of heart worms, prevalent among experimental animals in the Gulf Coast area. This parasite which is transmitted through mosquitoes was present in approximately 60 per cent of the animals. Many of the dogs that died during the first 24 hours after surgery were found to have a mass of worms filling the pulmonary artery which may have contributed to the early death of the animal.

The successful use of the patch technique as an adjunct to human coronary endarterectomy was demonstrated by the autopsy study. The arteriograms made following endarterectomy and closure of the vessel with a patch consistently demonstrated an increase in diameter.

Another possible application of the patch technique to coronary surgery which warrants further consideration is in vessels with only partial occlusion. In such cases a longitudinal incision might be made over the narrow segment and a patch sewn to the margins of the incision to increase the diameter of the vessel. This would obviate the need for endarterectomy, leaving the intima intact and thus avoiding the possible complication of plaque elevation and distal dissection. Clinically this technique has been used successfully in small caliber arteries such as popliteal, carotid, vertebral, and renal vessels with occlusive disease.

SUMMARY

This study consists of an evaluation of the patch technique as an adjunct to coronary endarterectomy. Patches made from arterial autograft, venous autograft, pericardial sac, and Dacron prosthesis were successfully used to facilitate closure of longitudinal incisions in the circumflex branch of the left coronary in dogs. The best results were obtained with arterial autograft, maintaining patency in 7 out of 10 animals.

Application of the technique to the coronary arteries in human beings was evaluated in autopsy hearts in which an endarterectomy was performed for segmental occlusive disease. The longitudinal arteriotomy incisions in the

vessels were closed with a patch thus avoiding narrowing. The patch technique without endarterectomy may be a satisfactory technique for surgical treatment of partial occlusions of the coronary vessels.

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A STUDY OF ACID-BASE AND ELECTROLYTE DERANGEMENTS AFTER PROLONGED CARDIOPULMONARY BYPASS

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THE development of metabolic acidosis during cardiopulmonary bypass has been noted by many observers,[1, 2] and remains a possible serious complication of extracorporeal circulation. Bicarbonate added during bypass,[3] high perfusion rates,[4] and utilization of 98 per cent oxygen and 2 per cent carbon dioxide as the oxygenating mixture have all been used to reduce the incidence and severity of this acidosis. Hypothermia,[6] even with low flow rates, has been demonstrated to prevent the development of metabolic acidosis.

Various electrolyte changes have been noted[4] during bypass, with no apparent fixed pattern of rise or drop. Respiratory compensation or aggravation of the acidosis must be considered in the development of acid-base derangements.

A study of the results of prolonged perfusion, when bicarbonate is added during the perfusion, with 98 per cent oxygen and 2 per cent carbon dioxide used as the oxygenating gas, and when high flow rates are used, would be of value. The interrelationships between acid-base disturbances and electrolyte changes can be studied simultaneously under these conditions. It is the purpose of this paper to present the results of a series of experiments with these facts in mind.

MATERIAL AND METHODS

Adult mongrel dogs, weighing 13 to 20 kilograms, were used. Preoperative medication of 50 mg. of Dermerol and 1 mg. of atropine was given 1 hour before operation. The animals were anesthetized lightly with Pentothal sodium, an endotracheal tube was inserted, and they were placed on an automatic res-

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pirator, using compressed air. The right hemithorax was opened through the fourth interspace. Both femoral arteries were exposed and a Teflon catheter suitable for the systemic return was placed into the left femoral artery. A polyethylene catheter was placed in the right femoral artery for monitoring blood pressure and for blood sampling. This catheter was left in place until 5 to 6 hours post-perfusion when the last specimen was taken. The left femoral vein was cannulated for venous pressure determination and for adding drugs.

Venous return to the pump was through a large catheter placed in the right atrium through the appendage, with the pulmonary artery occluded with a Rumel tourniquet. Two milligrams of heparin per kilogram of body weight were given before the catheter was inserted and 4 mg. of protamine per kilogram at the end of the perfusion.

The blood was drained into a reservoir placed below the level of the operating table and pumped into a Kay-Cross rotating disc oxygenator through a Sigma-motor pump. A nine-inch oxygenator was used and the discs were set at 90 r.p.m. An oxygen-carbon dioxide mixture of 98 per cent O_2 and 2 per cent CO_2, flowing at 6 L. per minute, was used as the oxygenating gas. A heat exchanger unit, set at 101° C., was placed in the arterial line, which in turn was inserted into the left femoral artery. Temperature was monitored through an esophageal probe placed in the mid-esophagus. All animals were maintained at 98° to 100° C. throughout the perfusion.

Freshly drawn, untyped, heparinized blood was used for priming the system. Arterial blood specimens were collected in heparin syringes for determination of pH, CO_2 potassium (K), chloride (Cl), and sodium (Na), and some were studied for plasma hemoglobin and O_2 saturations. These determinations were done before, during, and immediately after the perfusion, and at hourly intervals for 5 hours thereafter.

The perfusions were carried out for 60 to 90 minutes. The flow rate for all cases was 80 to 100 c.c. per kilogram per minute. Twenty-five cubic centimeters of sodium bicarbonate (22 mEq.) were added to the venous reservoir for every 20 minutes of perfusion. When the perfusion was terminated, the incisions were closed except for the right femoral incision. The femoral catheters were removed 5 hours after the last specimen was taken. All animals were given penicillin for 3 days after the perfusion. Animals were taken off the respirator as soon as the chest was closed.

The first series of experiments were designed to study the efficacy of the system. Plasma hemoglobin values and arterial O_2 saturations of the pre- and post-perfusion specimens were studied. When the efficacy of the system was demonstrated, animals were perfused for 60 and 90 minutes for survival, pH, CO_2, and electrolyte studies.

pH determinations were carried out on a Cambridge Research model pH meter, using a constant temperature water bath set at 37° C. Carbon dioxide and oxygen saturations were determined by the Van Slyke method. Electrolytes were determined with a flame photometer. Bicarbonate and pCO_2 values were calculated from appropriate nomograms.[7]

RESULTS

a. *Control Group.*—Studies of oxygen saturations and plasma hemoglobin levels after 40 to 90 min. of perfusion showed adequate post-perfusion oxygenation and only mild increases in plasma hemoglobin levels (Table I). It was, therefore, our opinion that our perfusion system was adequate.

TABLE I. OXYGEN SATURATION VALUES BEFORE AND AFTER BYPASS AND PLASMA HEMOGLOBIN VALUES AFTER BYPASS

DOG NO.	DURATION OF PERFUSION (MIN.)	POST-PERFUSION PLASMA HB (MG. %)	OXYGEN SATURATION (%)	
			PRE-PERFUSION	POST-PERFUSION
1	40	230	96.6	101.4
2	50	320	95.2	99.2
3	60	210	97.3	96.4
4	90	245	96.4	99.2
5	90	205	97.2	96.6
6	90	80	92.0	96.4

b. *Prolonged Perfusion Group.*—Of 9 animals perfused for 1 hour, 7 lived and 2 died. Of 7 animals perfused for 1½ hours, 3 lived and 4 died (Table II). The deaths were all characterized by progressive drop in blood pressure, loss of reflexes, hyperventilation, and death within 5 hours after the perfusion was terminated. On postmortem examination, there was no hemorrhage, atelectasis, or other obvious cause of death.

TABLE II. SURVIVAL AMONG ANIMALS STUDIED, PERFUSED FROM 60 TO 90 MINUTES

NO. OF DOGS PERFUSED	DURATION OF PERFUSION (MIN.)	NUMBER OF SURVIVORS
9	60	7
7	90	3

From Tables III and IV it is obvious that the animals that died had a progressive acidosis and a progressive drop in base bicarbonate. The survivors maintained a normal pH with only minor fluctuations of base bicarbonate. In some cases, the addition of bicarbonate during the perfusion caused an alkalosis at the termination of the perfusion which returned to normal values in a few hours. Acidosis was more prevalent and more severe in the animals perfused for 1½ hours than in those perfused for 1 hour.

The base bicarbonate was decreased before an obvious change in pH took place. A progressively falling base bicarbonate indicated a progressive acidosis, as is demonstrated in animals Nos. 20, 21, and 22. The values in Dog 15 illustrate the gradual development of acidosis with a progressive drop in bicarbonate. Dogs 14 and 19 show the rapid drop in pH over a period of 1 hour when the base bicarbonate is low (13 mEq. and 18 mEq., respectively).

Dogs 15, 20, 21, and 22 demonstrate that the finding of a normal pH and base bicarbonate at the end of the perfusion does not preclude the development of acidosis 3 to 5 hours after the termination of the perfusion.

The animals that died had pCO_2 values which were normal or low (see

TABLE III. COMPARISON OF pH AND BASE BICARBONATE LEVELS IN SURVIVORS AND NONSURVIVORS AFTER 1 HOUR OF PERFUSION

	IMMEDIATE POST-PERFUSION		ONE HOUR POST-PERFUSION		TWO HOURS POST-PERFUSION		THREE HOURS POST-PERFUSION		FOUR HOURS POST-PERFUSION		FIVE HOURS POST-PERFUSION	
NO.	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*
					Survivors							
7	7.31	16	7.50	18	7.36	19	7.24	20	7.20	18	7.30†	25†
8	7.37	25	7.24	21	7.27	22	7.36		7.42	21	7.44	19
9	7.51	23	7.45	21	7.30	25						
10	7.30	18	7.47	17	7.48	23	7.30	23	7.30	25	7.50	27
11	7.53	19	7.55	17	7.35	20	7.47	19	7.37	23	7.34	21
12	7.50	20	7.47	20	7.45	20	7.33†	24†	7.35	22	7.38	20
13	7.40	18	7.45	17	7.35	17	7.41	18	7.38	17		
					Nonsurvivors							
14	7.53	13	7.10	6	7.15	7						
15	7.45	27	7.50	21	7.50	17	7.35	15	7.10			

*Base bicarbonate in mEq./L.
†25 c.c (22 mEq.) of sodium bicarbonate ($NaHCO_3$) were added.

TABLE IV. COMPARISON OF pH AND BASE BICARBONATE LEVELS IN SURVIVORS AND NONSURVIVORS AFTER 90 MINUTES OF PERFUSION

	IMMEDIATE POST-PERFUSION		ONE HOUR POST-PERFUSION		TWO HOURS POST-PERFUSION		THREE HOURS POST-PERFUSION		FOUR HOURS POST-PERFUSION		FIVE HOURS POST-PERFUSION	
NO.	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*	pH	$BHCO_3$*
					Survivors							
16	7.59	25	7.53	25	7.41	25	7.40	24	7.40	23		
17	7.53	27	7.62	21	7.45	24	7.25		7.48	24		
18	7.43	20	7.39	21	7.14		7.35		7.39		7.45	
					Nonsurvivors							
19	7.30	18	7.00	14								
20	7.25	13			7.10	10	7.12†		7.14		7.00	
21	7.50	20	7.45	14	7.33	11						
22	7.30	18	7.31	18	7.10	15						

*Base bicarbonate in mEq./L.
†50 c.c. (44 mEq.) of sodium bicarbonate ($NaHCO_3$) were added.

Tables V and VI), indicating that the acidosis was not respiratory, but a true metabolic acidosis. Many had low pCO_2 values, indicating an attempt at respiratory compensation. There was no superimposed respiratory acidosis in any of the animals.

Most of the pCO_2 values immediately post-perfusion were low (Tables V and VI), demonstrating the ability of the oxygenator to eliminate CO_2. The pCO_2 gradually rose during the 5 hours in which the animal was observed and were close to normal values at the end of 5 hours.

The Na and Cl values changed little, except for an increase in Na immediately after the termination of the perfusion, undoubtedly due to the saline in the priming blood.

The K values showed some interesting changes. Most of the values fluctuated only slightly, but some showed marked lowering and elevation. In Dog 7 the K was 2.0 mEq. per liter when the pH was 7.50 and remained low until potassium chloride was added. Dog 9 showed a K value of 2.0 when the pH

TABLE V. COMPARISON OF CO_2 AND pCO_2 VALUES IN SURVIVORS AND NONSURVIVORS AFTER 1 HOUR OF PERFUSION

NO.	PRE-PERFUSION		IMMEDIATE POST-PERFUSION		ONE HOUR POST-PERFUSION		TWO HOURS POST-PERFUSION		THREE HOURS POST-PERFUSION		FOUR HOURS POST-PERFUSION		FIVE HOURS POST-PERFUSION	
	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)
Survivors														
7	35.4	38	38	34	42.8	24	44.7	36	47.5	50	42.8	47	62*	70*
8	50	44	59.6	50	51.3	52	52.4	51			48.4	34	43.8	25
9	57.6	41	52.9	30	50.2	32	50.4	52						
10	40	27	42.8	37.5	40	24	55	33.5	58.5	53	60.5	57	64.1	38
11	39	21	44.1	23	40.5	20	47.8	40	45	28	50.7	38	50.3	40
12	42	23.5	48.4	23	48.4	30	48.4	31	59.5*	50*	54.9	46	66	53
13	39.1	24.5	41.9	30	39.1	24	39.1	31	41	28	39.1	29		
Nonsurvivors														
14	32.7	20	30.8	26	14.9	19	16.7	18						
15	44.7	24	62.4	43.5	49.4	28	38.2	22	36.4	26.5				

*25 c.c. (22 mEq.) of sodium bicarbonate ($NaHCO_3$) were added.

TABLE VI. COMPARISON OF CO_2 AND pCO_2 VALUES IN SURVIVORS AND NONSURVIVORS AFTER 90 MINUTES OF PERFUSION

	PRE-PERFUSION		IMMEDIATE POST-PERFUSION		ONE HOUR POST-PERFUSION		TWO HOURS POST-PERFUSION		THREE HOURS POST-PERFUSION		FOUR HOURS POST-PERFUSION		FIVE HOURS POST-PERFUSION	
NO.	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)	CO_2 (VOL. %)	pCO_2 (MM. Hg)
						Survivors								
16	41	24	55.4	28	59.1	31	60	39	56.4	42	54.5	49		
17			61.5	34	50.2	21.5	56.7	37						
18	47.1	25	69.8	49										
						Nonsurvivors								
19	35.4	28	44.7	40	35.4	53								
20	35.8	27	30.3	30			25.7	34						
21	47.4	30	46	26	34	20	25.7	20						
22	39.1	24.5	43.7	39	41.9	37	37	50						

TABLE VII. COMPARISON OF ELECTROLYTES IN SURVIVORS AND NONSURVIVORS AFTER 1 HOUR OF PERFUSION*

	PRE-PERFUSION			IMMEDIATE POST-PERFUSION			1 HOUR POST-PERFUSION			2 HOURS POST-PERFUSION			3 HOURS POST-PERFUSION			4 HOURS POST-PERFUSION			5 HOURS POST-PERFUSION		
NO.	K	Na	cl	K	Na	cl	K	Na	cl	K	Na	cl	K	Na	cl	K	Na	cl	K	Na	cl
Survivors																					
7	3.8	138	117	3.5	142	114	2.0	140	105	1.8	142	110	2.2			2.6			5.3†		
8	3.8	140	108	2.3	136	105	2.3	140	107	2.2	144	110	3.0	140	108	3.1	134	105	5.2	137	
9	2.7	145		2.0	149		2.1	140		2.3	140										
10	2.7			3.2			3.2			2.6			2.6			2.8			2.6		
11	2.6	137	111	2.5	136	113	2.5	148	114	2.4	145	114	2.8	140	114	4.1	143		4.2	134	
12	3.3	154		2.9	140		3.2	151		3.1	148		3.2‡	152‡		4.1	148		3.7	151	
13	2.2	138	108	2.5	141	116	3.4	151		3.4	149		3.4	143	115	2.7	158	120			
Nonsurvivors																					
14	2.5	139	104	4.5	148	112	5.5	135	97	6.9	131										
15	3.1	138		3.1	147		3.4	140		3.4	143		3.4	149							

*Values are in mEq./L.
†One ampule KCl and 25 c.c. (22 mEq.) of sodium bicarbonate ($NaHCO_3$) were added.
‡25 c.c. (22 mEq.) of sodium bicarbonate ($NaHCO_3$) were added.

TABLE VIII. COMPARISON OF ELECTROLYTES IN SURVIVORS AND NONSURVIVORS FOLLOWING 90 MINUTES OF PERFUSION*

	PRE-PERFUSION			IMMEDIATE POST-PERFUSION			1 HOUR POST-PERFUSION			2 HOURS POST-PERFUSION			3 HOURS POST-PERFUSION			4 HOURS POST-PERFUSION			5 HOURS POST-PERFUSION		
NO.	K	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl
Survivors																					
16	3.0	136	113	2.6	146	113	2.3	141	110	3.1	140		2.9	140	111	2.8	136				
17				2.1	148	115	2.8	180	124	3.2†	161	118	7.1	157		4.4	157	123			
18	2.7	141		2.6	153		2.4	142		2.6			3.0			3.0					
Nonsurvivors																					
19	3.9			3.2			4.1														
20	2.1	137		3.7	141				.	5.2	148		3.9‡	140		3.8					
21	2.9	140	110	3.7	154	114	3.7	149	111	4.2	148	120									
22	3.3	140	130	3.4	136	115	3.2	137	112	4.5	135										

*Values are in mEq./L.
†One ampule of KCl added to intravenous solution.
‡25 c.c. (22 mEq.) of sodium bicarbonate ($NaHCO_3$) were added.

TABLE IX. pH, BICARBONATE LEVELS, AND CO_2 VALUES IN 17 CASES OF CARDIOPULMONARY BYPASS AT 25° TO 30° C.

PATIENT	DEFECT	LENGTH OF PERFUSION		pH	$BHCO_3$	CO_2	pCO_2
1. W. R.	Interventricular septal defect	51 min.	pre-perf.	7.56	21.5	49.6	25
			post-perf.	7.47	15.8	35.6	22.5
			5 hr. post-perf.	7.45	22.5	53.4	34.5
2. R. M.	Pulmonic stenosis	21 min.	pre-perf.	7.40	20	47	34
			post-perf.	7.33	19	45.2	38
			5 hr. post-perf.	7.37	19.5	47.1	36.5
3. R. R.	Interatrial septal defect	21 min.	pre-perf.	7.43	24.5	56.8	40
			post-perf.			53	
			5 hr. post-perf.	7.30	21	49.3	43
4. M. B.	Mitral insufficiency	50 min.	pre-perf.	7.48	26	63.3	38
			post-perf.	7.45	21	49.3	32
			5 hr. post-perf.	7.40	22	52.1	38
5. R. C.	Interatrial septal defect	30 min.	pre-perf.	7.50	24.5	36	20
			post-perf.	7.55	22.2	41.7	21
			5 hr. post-perf.	7.40	20.5	48.3	35.5
6. H. G.	Aortic stenosis	78 min.	pre-perf.	7.55	22	50.9	26
			post-perf.	7.50	17.8	41.4	23
			5 hr. post-perf.	7.35	17	39.6	32
7. M. R.	Interventricular septal defect	58 min.	pre-perf.	7.35	23.5	57.4	47
			post-perf.	7.40			
			5 hr. post-perf.	7.35	19	45.2	36.5
8. J. W.	Aortic stenosis Pulmonic stenosis	53 min.	pre-perf.	7.48	20.8	48.7	29
			post-perf.	7.47	21	48.7	30
			5 hr. post-perf.	7.40	21	50.5	37
9. J. H.	Interventricular septal defect	105 min.	pre-perf.	7.62	17.8	40.7	17.2
			post-perf.	7.50	17.1	39.7	22.2
			5 hr. post-perf.	7.43	24	57.3	37.5
10. B. T.	A-V canal	72 min.	pre-perf.	7.54	22.5	52.2	27.2
			post-perf.	7.52	20.0	47.5	27.2
			5 hr. post-perf.	7.38	24.0	57.7	45

was 7.51. Dog 11 showed a K of 2.5 at a pH of 7.53 which rose to 4.1 at a pH of 7.37. Dog 12 showed a K of 2.9 at a pH of 7.50 and a K of 4.1 when the pH fell to 7.35. In Dog 14 the K was 5.5 and 6.9 terminally when the pH was 7.1. In Dog 20 the K was 5.2 at a pH of 7.10 which then dropped to 3.8 as the sodium bicarbonate was added.

These variations in K with changes in pH are undoubtedly the result of addition of large amounts of sodium bicarbonate and the formation of large amounts of fixed acids. There is a known relationship between K and pH.[8-11] The fluctuations in K seen in these animals is a result of the entry of K^+ into the cells to replace H^+ released by the cells into the extracellular space during alkalosis, and the shift of K^+ out of the cells when H^+ enters the cells from the extracellular space during acidosis.

c. *Clinical Studies.*—Analysis of Table IX, presenting the studies carried out in our human cases performed under hypothermia (25° C. – 30° C.), demon-

TABLE IX. CONT'D

PATIENT	DEFECT	LENGTH OF FUSION		PH	$BHCO_3$	CO_2	PCO_2
11. C. S.	Interatrial septal defect	20 min.	pre-perf.	7.40	25.0	59.1	43
			post-perf.	7.38	21.5	51.7	39
			5 hr. post-perf.	7.42	22.5	53.6	37.5
12. G. T.	Ostium primum	63 min.	pre-perf.	7.40	18	42.6	31
			post-perf.	7.45			
			5 hr. post-perf.	7.45	24	58.6	40
13. G. G.	Aortic stenosis (subaortic)	48 min.	pre-perf.	7.44	20	48	31
			post-perf.	7.40	20.5	48	35
			5 hr. post-perf.	7.40	26	62.7	47
14. J. R.	Interventricular septal defect	80 min.	pre-perf.	7.60	20	45.6	21
			post-perf.	7.45	23	54.8	35.5
			5 hr. post-perf.	7.45	24	56.5	37
15. J. H.	Total anomalous venous drainage	120 min.	pre-perf.	7.30	12.5	29.2	25
			post-perf.	7.26	22	52.9	54 (H_2CO_3-1.6)
			2 hr. post-perf.	7.40	(venous blood)		
			6 hr. post-perf.	7.25 (venous blood)	24.5	60	66 (H_2CO_3-1.98)
16. R. S.	Interatrial septal defect	39 min.	pre-perf.	7.60	19.5	44.7	20
			post-perf.	7.50	20	46.5	27
			5 hr. post-perf.	7.55	22.5	52.1	26.5
17. D. G.	Interventricular septal defect	57 min.	pre-perf.	7.45	19	44.7	28
			post-perf.	7.25	21.2	52.1	52 (H_2CO_3-1.6)
			5 hr. post-perf.	7.45	27	63.6	42 (H_2CO_3-1.3)

strates that not one instance of true metabolic acidosis developed, even in very prolonged perfusions. Undoubtedly, the hypothermia is in large part responsible for this.[4]

The pCO_2 was low in most cases, both before and after the perfusion, when the patient was anesthetized and being ventilated by the anesthetist. Five hours after termination of the perfusion, the pCO_2 approached normal and the patient was regulating his own respirations. In all these cases, 25 c.c. of sodium bicarbonate (22 mEq.) were added to the venous reservoir for every 15 minutes of bypass.

Case 15 (J. H.) is very unusual and demonstrates the importance of considering CO_2 values in conjunction with pH. The patient was a 3-year-old male with total anomalous venous drainage. Before perfusion, at the time when the first sample was taken, the child's temperature was 41° C. (105° F.) The blood pressure was 60 to 70 mm. Hg. The pH was 7.30 with a base bicarbonate value of 12.5 mEq. per liter, i.e., a true metabolic acidosis. This is due to a poor circulatory status in conjunction with a temperature of 41° C., when

the patient is metabolizing at an accelerated rate which leads to anoxic oxidation with production of fixed acids. The patient was being hyperventilated and the pCO_2 was low.

During the perfusion, the body temperature was kept at 25° C. during the repair, and then rewarmed to 37° C. One hundred cubic centimeters of sodium bicarbonate (88 mEq.) were added during the perfusion. After the perfusion, the patient developed pulmonary edema and the post-perfusion specimens were taken at that time. Although the pH was 7.26, the base bicarbonate was 22 mEq. per liter. The CO_2 value of 52.9 vol. per cent and pCO_2 of 54 mm. Hg, together with a calculated carbonic acid value of 1.6 indicates a failure to eliminate CO_2, which was causing a respiratory acidosis. No bicarbonate was given and by hyperventilation alone the pH of the venous blood was raised to 7.40. Later, when the child developed pulmonary edema again, respiratory acidosis developed again with CO_2 of 60 vol. per cent and pCO_2 of 66 mm. Hg with a calculated carbonic acid value of 1.98.

Case 17 (D. G.) also demonstrates a respiratory acidosis after the perfusion.

DISCUSSION

Many authors have stressed the importance of maintaining high flow rates to prevent the development of metabolic acidosis which is so often seen at low flow rates. Cross and Kay[12] and Clowes[13] and their associates have observed a fall in pH and blood buffer base during extracorporeal circulation and thought that this metabolic acidosis was due to "circulatory stasis." They also pointed out that a metabolic acidosis was present in the priming blood.

During the bypass, even at high perfusion rates, the total flow is below resting cardiac output and therefore the tissues are not adequately oxygenated, and anaerobic oxidation takes place. Under these conditions high lactic and pyruvic acid levels develop in the blood, giving a true metabolic acidosis. The body corrects this by its buffer systems; namely, bicarbonate, phosphate, and hemoglobin buffer systems, and by shifts of Na and K. A reduction in base bicarbonate indicates an excess of organic acids which neutralize these buffers. This accumulation of acids results from the combined effects of poor blood flow and increased rate of production in anoxic tissues. Iwao[14] has shown that with balloons inflated around the venae cavae to reduce the cardiac output, with a blood pressure of 45 mm. Hg, all animals will develop severe metabolic acidosis.

The hydrogen ion in this acidosis arises within the cell itself, apparently on the basis of inadequate flow, and the intracellular buffers are taken up first. This is in sharp contrast to renal acidosis or that caused by the infusion of ammonium chloride or fixed acids. In these cases the extracellular buffers are taken up first and the changes in the cells occur later.

During bypass, the pH is maintained within relatively normal limits by the ability of the oxygenator to eliminate CO_2. There appears to be a decrease of this function during prolonged perfusions. Base bicarbonate falls in a regular fashion during perfusion.

The relationship of flow rate to acidosis has been shown by Pontius[15] and Clowes.[13] Pontius studied a group of experimental animals in which the perfusion rates were increased from 20 to 30 c.c. to 60 to 150 c.c. per kilogram per minute. The corresponding average values of change in buffer base ranged from –6.4 mEq. per liter to –2.1 mEq. per liter.

Acidosis must be looked for soon after the perfusion and especially 3 to 5 hours after the perfusion. It is the late acidosis which causes many of the "sudden deaths" seen in the recovery room. When the anesthesia is completed and the pH is no longer corrected by overventilation, acidosis, which is metabolic and continuous, becomes manifest. This sudden death may be due to an elevation of serum K as will be discussed.

pH values alone[16] are unreliable as an index of post-perfusion acidosis, because of respiratory and blood buffer compensation. These values may be normal for a few hours after the perfusion and acidosis will still progressively develop. Within a few hours after perfusion, base bicarbonate levels begin to fall and that of pH soon follows. The tissues continue to form fixed acids even after perfusion has been discontinued. The damage to the tissues and to their enzymes, caused by prolonged or low flow perfusions, is often irreversible and fixed acids continue to be produced despite an adequate post-perfusion cardiac output and the addition of sodium bicarbonate. If the operation has not corrected the defect and the heart has not been improved by the procedure, acidosis is rapid in its appearance and is irreversible. A progressive drop in base bicarbonate, even with normal pH values, is an indication of a progressive metabolic acidosis.

The reason for the development of acidosis in one animal and its absence in another, perfused under the same conditions, at the same flow rate, and for the same length of time maintaining a similar blood pressure, is not clear. The same perfusion rate is obviously adequate for one animal but sub-basal for the other, and while one was evidently receiving adequate tissue oxygenation, the other was not.

The length of perfusion has a direct relationship to the development of acidosis. A short perfusion, even with low flow rates, allows the body to compensate for the tissue anoxia. Short perfusions, using low flow rates according to the "azygous flow" principle, will not develop acidosis, while longer perfusions, at these low flow rates, will. As better oxygenator systems are developed the safe limit for perfusion will be prolonged.

Our results show that the acidosis is purely metabolic and is not due to respiratory failure to remove CO_2. All the animals which died had low pCO_2 values indicating an attempt at compensation. The clinical cases all show low pCO_2 values, intentionally reduced by overventilation at the hands of the anesthetist. If respirations are impaired by collapse or secretions, the superimposed respiratory acidosis aggravates that present as a result of perfusion.

Scribner[8, 11] and others[9, 10] have clearly demonstrated the relationship between serum K and pH and that the internal equilibrium of K is in part a function of pH. The study of infusion of HCl in nephrectomized dogs[9] demonstrated that 40 per cent of the acid is neutralized by extracellular bicarbonate,

10 per cent by red blood cell buffers, and 50 per cent by diffusion of Na and K into the extracellular fluid. They suggested the exchange of extracellular H^+ for intracellular Na^+ and K^+ to account for the increase in extracellular Na and K. Thus acidosis increases and alkalosis decreases K, independent of changes in the total body K. Giebisch, Berger, and Pitts[10] have demonstrated that in respiratory acidosis and alkalosis Na^+ and K^+ were exchanged mole for mole for H^+ ion.

The data in our experiments demonstrate this interrelation between pH and K. The addition of sodium bicarbonate to neutralize an internal production of acids is not quantitative and the K will reflect the pH at any given time. This must be considered in the patient who has had open-heart surgery and when bicarbonate or another base is used to correct an acidosis that is present. These changes are independent of renal action. Many deaths seen in the patient who is acidotic may be a result of an elevated serum K.

Our clinical material demonstrates the beneficial effects of hypothermia in preventing acidosis. Although some of the perfusions were over 1½ hours long, in not one instance was acidosis present. The perfusion rate was 40 to 50 c.c. per kilogram per minute at the low temperatures and 80 to 90 c.c. per kilogram per minute at 37° C. Only mild depressions in plasma bicarbonate were noted and then returned to control levels at the end of 5 hours.

SUMMARY AND CONCLUSIONS

1. A group of dogs was subjected to total cardiopulmonary bypass for 60 to 90 minutes in duration. The procedures were carried out at high flow rates, at a temperature of 36° to 38° C., using 98 per cent oxygen and 2 per cent carbon dioxide as the oxygenating gas, with the addition of sodium bicarbonate during the perfusion.

2. The survivors showed no drop in base bicarbonate and no acidosis. The nonsurvivors all died with progressive acidosis.

3. Base bicarbonate was an earlier and more accurate indication of acidosis than the pH.

4. The respiratory contribution to the acidosis was minimal, and the pCO_2 values were low.

5. Acidosis must be looked for 3 to 5 hours after perfusion, even if there was no acidosis at the termination of the perfusion.

6. Hyperkalemia associated with acidosis and hypokalemia associated with alkalosis has been demonstrated and must be looked for in the patient subjected to total body perfusion.

7. Data on 17 human cases in which hypothermia was used in conjunction with the perfusion are presented. In no instance was acidosis present, even after long perfusions.

The authors wish to acknowledge the technical assistance of Dagnia Leja, Norman Fitz, and Dr. Albert S. Welberry.

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ANOMALOUS CORONARY ARTERY DISTRIBUTION ASSOCIATED WITH TETRALOGY OF FALLOT: A HAZARD IN OPEN CARDIAC REPAIR

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ANOMALOUS distribution of the coronary arteries in tetralogy of Fallot is of considerable importance. Recently reports have described the accidental division of a major coronary artery during open cardiac repair of this anomaly. This report describes the various patterns of distribution of the coronary arteries in tetralogy of Fallot with emphasis on surgical implications.

MATERIALS AND METHODS

The coronary artery distribution was studied in 22 specimens from cases of tetralogy of Fallot. Coronary artery injection studies, using a latex-barium sulfate mass, were performed on fresh specimens. X-rays were made of these hearts and the specimens were subsequently cleared. Gross dissection of the major coronary vessels was performed on formalin-fixed specimens. Similar studies were performed on 10 normal hearts.

RESULTS

The most consistent variation observed in this group was the increased vascularity of the right ventricle (Figs. 1 and 2). The infundibular branch of the right coronary was unusually prominent in all cases. This branch coursed directly across the area of the right ventricular outflow tract. In 18 normal hearts, the infundibular artery was relatively short, terminating high on the right ventricular surface (Fig. 1). The over-all pattern of distribution of the coronary arteries was found to be normal in 21 of 22 specimens examined.

An anomalous coronary artery distribution was found in 1 case. The coronary ostia were normally situated, and the right coronary artery followed a normal course. The left coronary artery, after arising from the left anterior

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sinus of Valsalva, turned immediately to the right and coursed between the aorta and pulmonary artery. It then passed around and in front of the pulmonary artery, coursing deep within the myocardium and continued around the left atrioventricular groove. The infundibular branch of the right coronary artery was enlarged and crossed the outflow tract of the right ventricle (Fig. 3).

Fig. 1.—Injection study of the vascular pattern of the cleared normal right ventricle. The coronary arteries were injected with a latex-barium suspension. A photograph of the anterior wall of the right ventricle is shown on the left, and a drawing from the original photograph is illustrated on the right. The usual site of a right ventriculotomy lies in an avascular area.

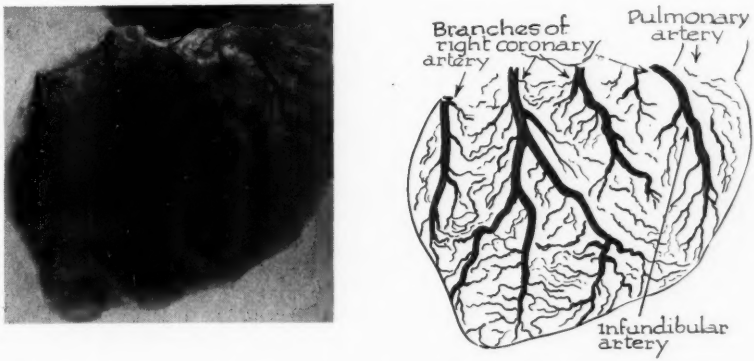

Fig. 2.—Latex-barium injection study of the vascular pattern of the cleared right ventricle in a specimen of tetralogy of Fallot. The photograph is shown at the left and a drawing from the original photograph is illustrated on the right. A marked increase in vascularity is apparent.

DISCUSSION

Although anomalous coronary artery distribution usually is considered of no clinical significance,[1] it does represent a potential hazard in cardiac surgery. The reports of accidental division of a major coronary artery during open repair of tetralogy of Fallot attest to the importance of anomalies of coronary circulation.

Senning[5] reported 5 cases in which an anomalous coronary artery coursed

directly across the right ventricular outflow tract, preventing the usual ventriculotomy incision. In 2 patients the descending interventricular artery originated from the right and coursed directly across the infundibulum. In 1 case the entire left coronary artery originated from the right coronary and coursed within the myocardium across the region of the infundibular stenosis. This artery was incised, and the patient died immediately.

Friedman[2] reported a case of tetralogy of Fallot with an anomalous single coronary artery. A major branch of a single right coronary artery, which proved to have the distribution of a normal left coronary artery, coursed over the outflow tract of the right ventriele to supply the left ventricular myocardium. This branch was divided during the right ventriculotomy, resulting in immediate death of the patient.

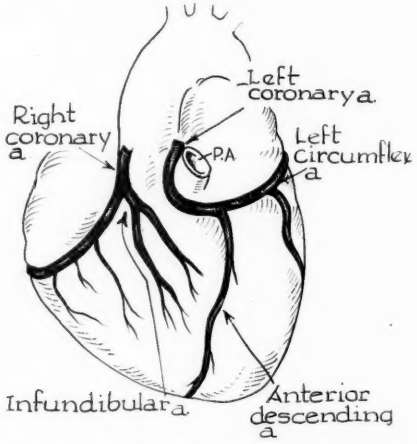

Fig. 3.—Drawing of case in present series (see text). The left coronary artery passed in front of the pulmonary artery. In the course of the usual operation for tetralogy of Fallot, this vessel would be divided.

Kirklin[3] reported 4 cases of tetralogy of Fallot with anomalous coronary arteries complicating ventriculotomy. In 1 case an unrecognized single right coronary artery was present. From this vessel arose a large branch which crossed the outflow tract of the right ventriele. This branch, which presumably had the distribution of a normal left coronary artery, was divided with the incision, and the patient died at the end of the operation. This case appears to be similar to the fatal cases reported by Senning and Friedman. In 3 other cases, a large branch of the right coronary artery crossed the outflow tract of the right ventriele to become the anterior descending artery. In 1 case this branch was divided and the child died 48 hours after the operation. Autopsy revealed an infarct in the left ventriele. In the other 2 cases, division of this branch was successfully avoided. The postoperative death of 1 of these patients was attributed to other causes.

Instances of anomalous coronary artery distribution similar to that in our case have not been reported. Although the anatomic distribution was correct,

the course of the left coronary artery was anomalous. Originating from the left anterior sinus of Valsalva, it turned immediately to the right and coursed around and in front of the pulmonary artery. The various distributions of the anomalous coronary arteries which have been reported in association with tetralogy of Fallot are illustrated (Fig. 4).

Spitzer[6] and Lev[4] have described the anomalous coronary artery distribution associated with transposition of arterial trunks. In partial transposition with pulmonary hypoplasia, there is a resemblance to tetralogy of Fallot except that both the aorta and pulmonary artery arise primarily from the right ventricle. The aortic cusps are rotated in a counterclockwise direction (about 120 degrees) and the coronary arteries show an atypical pattern of distribution.

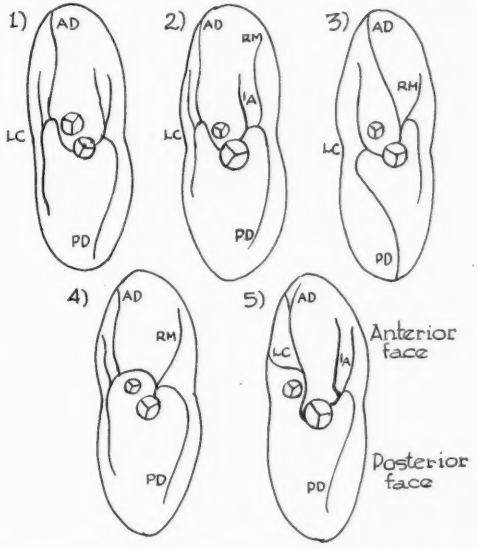

Fig. 4.—Drawing of various patterns of coronary artery distribution.
1, Normal heart. *AD*—anterior descending; *LC*—left coronary; *PD*—posterior descending.
2, Usual distribution in tetralogy of Fallot. The infundibular artery *(IA)* and right marginal *(RM)* are invariably enlarged.
3, Distribution seen in cases of extreme dextroposition of the aorta. The anterior descending artery arises from the right coronary.
4, Single coronary artery, with the left coronary passing in front of the pulmonary artery.
5, Distribution of coronary vessels in case included in present report. The left coronary arises in the normal position but passes in front of the pulmonary artery.

The anterior descending branch arises from the right coronary artery, while the posterior descending branch arises from the left coronary artery. In typical tetralogy of Fallot, the aortic cusps are displaced only 45 to 90 degrees in a counterclockwise position. The aorta emerges predominately from the left ventricle, and the over-all coronary artery distribution is usually normal. However, when the aorta arises largely from the right ventricle, the coronary artery distribution may resemble that of partial transposition, i.e., the anterior descending artery arising from the right coronary artery.

The infundibular artery, which is a preventricular branch of the right coronary artery, normally is relatively short and courses high on the right ventricular surface. In examining 22 cases of tetralogy of Fallot, this artery was consistently increased in length and caliber. It coursed completely across the outflow tract of the right ventricle and anastomosed freely with the left anterior descending artery.

To avoid division of a major coronary branch, the coronary distribution should be studied prior to ventriculotomy. Even careful inspection, however, may fail to reveal a coronary artery coursing deep within the myocardium. In such cases, temporary occlusion prior to extending the ventricular incision into the pulmonary artery may indicate the presence of an anomalous vessel. When the aorta is markedly dextropositioned, the anterior descending artery is particularly likely to arise from the right coronary artery.

SUMMARY AND CONCLUSIONS

1. The patterns of coronary artery distributions associated with tetralogy have been outlined.

2. The frequent origin of the anterior descending artery from the right coronary artery in cases of extreme dextroposition of the aorta has been emphasized.

3. An enlarged infundibular branch of the right coronary artery crossing the outflow tract of the right ventricle was observed in all cases of tetralogy. In addition, cases have been reported in which the left coronary or the anterior descending artery lie in front of the pulmonary artery. Division of such vessels has usually been fatal.

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PROFOUND HYPOTHERMIA AS AN ADJUNCT TO CARDIOVASCULAR SURGERY

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IT HAS BEEN demonstrated that selective cardiac hypothermia produced by coronary perfusion with cold, oxygenated blood results in periods of safe cardiac arrest.[1, 2, 3] Myocardial temperatures can be reduced by this method to the range of 5° to 20° C., permitting interruptions in coronary perfusion for periods of 15 to 25 minutes. Although the principle of hypothermic cardiac arrest has been accepted clinically, two factors tend to limit a general application of selective cooling in the field of cardiac surgery. First, spontaneous rewarming of the myocardium occurs, during the absence of perfusion, due to contact between the heart and the normothermic mediastinal structures. Additional heat from the operating room lights and the surgeon's hands further speeds the rewarming process. Second, a competent aortic valve is essential for successful coronary perfusion when accomplished by means of a catheter inserted into the proximal aortic arch.

On the basis of these undesirable features, laboratory investigations were undertaken to evaluate some of the physiologic effects of profound, generalized hypothermia (5° to 15° C.). It became apparent that this method also results in prompt hypothermic cardiac arrest, and allows prolonged periods of total circulatory arrest with minimal spontaneous rewarming. Furthermore, the success of total body cooling does not depend upon the presence of a competent aortic valve.

This report includes an evaluation of two methods for the production of profound hypothermia in the laboratory, and attempts to assess the physiologic effects of varying periods of hypothermic cardiac arrest and total circulatory arrest.

EXPERIMENTAL METHODS AND MATERIALS

Adult mongrel dogs of either sex, weighing 4 to 25 kilograms, were used. All animals were anesthetized with intravenous pentobarbital sodium, 30 mg.

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per kilogram, and intubated. Respirations were controlled with a Bennett respirator which delivered a peak positive pressure of 25 cm. of water. Polyethylene cannulas were inserted into the left femoral artery and femoral vein for measurement of mean arterial pressure and central venous pressure. These pressures were measured with a Statham pressure transducer and recorded with

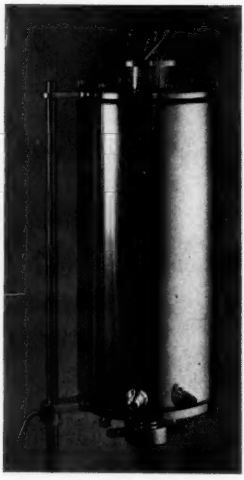

Fig. 1.—The heat exchanger in position on the pump oxygenator.

a Sanborn direct-writer recorder. Serial electrocardiograms and electroencephalograms were obtained in most animals, and recorded with a Sanborn Viso-Cardiette and a Grass 12 channel electroencephalograph (Model IIID).

Simultaneous myocardial, brain, and muscle temperatures were measured with thermocouples mounted on 22 gauge needles. The brain needle was inserted through a temporal burr hole created prior to the thoracotomy. Individual thermistors connected to a multiple channel telethermometer recorded temperatures in the mid-esophagus, rectum, and in the arterial and venous lines of the perfusion system. The temperature of the fluid entering and leaving the heat exchanger was also monitored by means of thermocouples mounted on 22 gauge needles.

A heat exchanger of our design with a capacity of 350 c.c. was utilized in all experiments.* The unit consisted of two end plates and a stainless steel jacket which was welded around 80 straight steel tubes (30.5 cm. in length and 0.5 cm. in diameter).[2] An air release valve and a Pyrex chamber were secured to the inflow end plate to facilitate priming of the unit (Figs. 1 and 2). All parts disassembled with ease to permit cleaning and sterilization. Water, or a water-alcohol solution, was circulated through the jacket of the heat exchanger at temperatures of 0.5° to 42° C.

*Constructed to our specifications by International Medical Instrument Company, Wakefield, Mass.

A bilateral anterior thoracotomy was performed in all animals; the chest was entered through the fifth interspace. Prior to arterial and venous cannulation, 1.0 mg. of heparin per kilogram of body weight was administered intravenously. At the conclusion of the experiment and following decannulation, an antiheparin compound (Polybrene [hexadimethrine]) was given in a one-to-one ratio. Profound hypothermia was produced in one group of dogs (Group I) during cardiopulmonary bypass. Cannulation of the venae cavae and insertion of catheters into the right and left auricles returned the systemic venous flow,

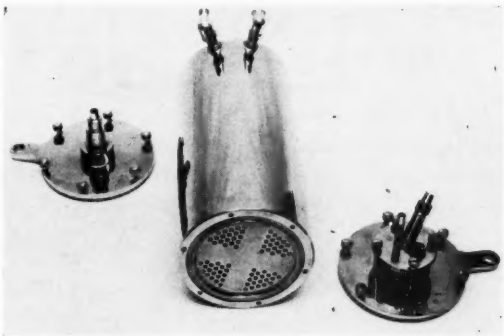

Fig. 2.—Component parts of the heat exchanger, partially assembled.

coronary sinus blood, and bronchial collateral flow to a Gross-model pump oxygenator system.[4] Oxygenated blood was then pumped through the heat exchanger to the right femoral artery of the animal, completing the bypass circuit.

The temperature of the priming blood (2,800 c.c.) was reduced to 2°-4° C. prior to bypass by recirculation through the heat exchanger for a 10-minute period. The start of each perfusion with this pre-cooled blood resulted in a very rapid reduction in esophageal, rectal, cardiac, and brain temperatures. In all experiments, cooling was terminated when the brain temperature reached a range of 8° to 15° C.

After an interval of total circulatory arrest, rewarming was begun by circulating warm fluid (42° C.) through the heat exchanger. Electrical defibrillation of the ventricles was accomplished when the cardiac temperature reached 30° C., and decannulation of the venae cavae was carried out at a rectal temperature of 32° to 35° C. A downward temperature drift of 2° to 3° usually occurred during closure of the thoracotomy, with eventual stabilization in the range of 30° to 32° C. Additional rewarming of the animal to a normal body temperature was allowed to take place spontaneously.

In a second group of animals (Group II), profound hypothermia was produced with the use of an extracorporeal circuit without an oxygenator. A left heart bypass was established by inserting a large fenestrated cannula through the left auricular appendage, mitral valve, and into the left ventricle. Pulmonary

venous blood was then pumped (Sigmamotor pump) from the auricle and ventricle into a 500 c.c. reservoir which served as a collecting chamber. The blood drained by gravity from here into a second, graduated reservoir which was coupled to the heat exchanger (Fig. 3). Flows were determined frequently by recording the volume of blood which collected in this reservoir when the tubing distal to the heat exchanger was occluded for periods of 10 to 30 seconds.

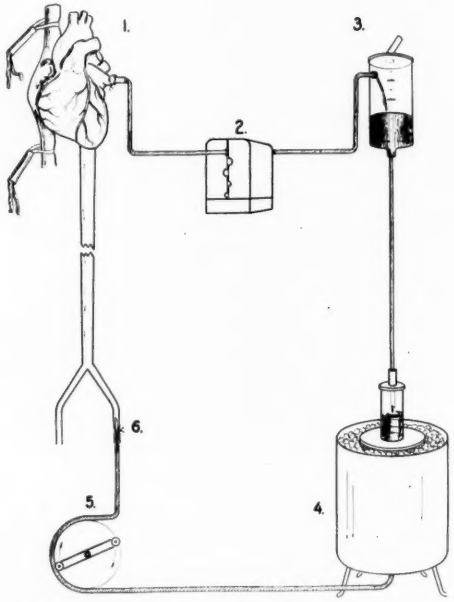

Fig. 3.—Diagrammatic representation of a left heart bypass (Group II) with the heat exchanger mounted in a cylindrical tank. Hot or cold fluid (0.5° C. to 42° C.) was pumped through the jacket of the unit to produce cooling or rewarming. A Therm-O-Rite unit coupled to the heat exchanger was also used for this purpose.

A De Bakey rotary pump was utilized to direct the flow of cold blood from the heat exchanger into the animal via a cannula in the right femoral artery. Inflation of the lungs with 98 per cent oxygen and 2 per cent carbon dioxide continued throughout the period of cooling and rewarming. Tapes were placed loosely around the venae cavae but were not occluded until circulatory arrest was produced at brain temperatures of 10° to 17° C.

During left heart bypass, the average blood flows ranged from 28 to 45 c.c. per kilogram per minute. The maximum flow values were noted, as expected, during the interval when the right ventricle continued to contract. After ventricular fibrillation and hypothermic arrest ensued, blood flow and the cooling rate rapidly decreased. Despite this fact, an advantage of the

method consisted of the small priming volume of blood required for each experiment (800 c.c. to 1,000 c.c.).

A period of total circulatory arrest, ranging from 25 to 60 minutes, was effected in each dog, and then rewarming was begun. Defibrillation of the heart and decannulation were accomplished in a manner similar to that used for Group I.

Certain metabolic observations were made during these experiments. A study of the oxygen utilization, pH changes, carbon dioxide content, and available buffer base was carried out in serial fashion after various intervals of total circulatory arrest. These data will be reported separately.

RESULTS

A. Efficiency of Cooling and Rewarming (Groups I and II).—In the animals of Group I, the mean duration of the cooling phase was 24 minutes (Fig. 4). Throughout this interval, the esophageal, cardiac, brain, rectal, and muscle temperatures decreased at rates varying from 1.2° C. per minute to 0.6° C. per minute (Table I). In all animals the rapidity of the cooling process was

TABLE I. THE DURATION AND RATE OF VISCERAL COOLING IN THE ANIMALS OF GROUPS I AND II*

	DURATION (MIN.)	VISCERAL TEMPERATURE CHANGES (° C. PER MIN.)				
		RECTUM	ESOPHAGUS	HEART	BRAIN	MUSCLE
Group I						
16 animals	24	0.80	1.20	1.00	0.90	0.60
Group II						
12 animals	40	0.40	0.56	0.50	0.48	0.30

*These data are mean figures.

directly proportional to the existing blood flow and perfusion pressure. The flow values ranged from 50 to 70 c.c. per kilogram per minute and the mean perfusion pressure varied from 100 to 136 mm. Hg. Both blood flow and perfusion pressure decreased coincidentally with the fall in body temperature, and increased during the rewarming phase (Table II).

TABLE II. THE DURATION AND REWARMING RATE IN THE ANIMALS IN GROUPS I AND II*

DURATION (MIN.)	VISCERAL TEMPERATURE CHANGES (° C. PER MIN.)				
	RECTUM	ESOPHAGUS	HEART	BRAIN	MUSCLE
		Group I (16 animals)			
40	0.45	0.90	0.95	0.60	0.25
		Group II (12 animals)			
48	0.35	0.47	0.56	0.45	0.30

*These data are mean figures.

Cooling proceeded at a slower rate in the dogs of Group II, with an average duration of 40 minutes (Fig. 5; Tables I and III). As a consequence of a low blood flow and perfusion pressure, the lowest temperatures recorded in this group of animals were 2° to 8° C. higher than those of Group I (Table IV).

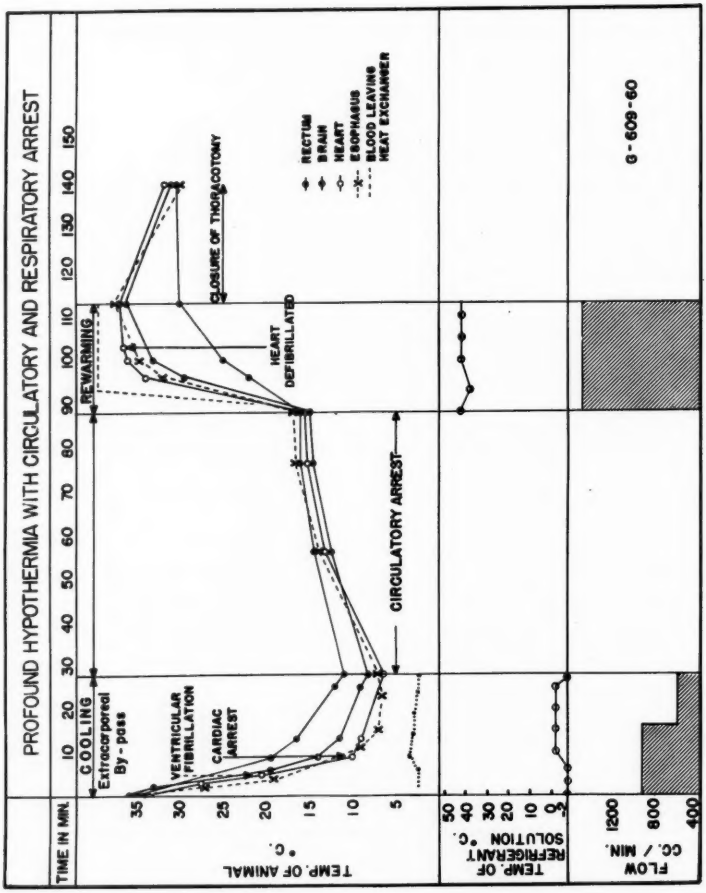

Fig. 4.—An illustration of the cooling and rewarming data from an animal of Group I.

The rewarming occupied an average of 40 minutes in the animals of Group I, and 48 minutes in those of Group II (Table II). Esophageal and cardiac temperatures increased rapidly with the perfusion of warm blood (40° C.),

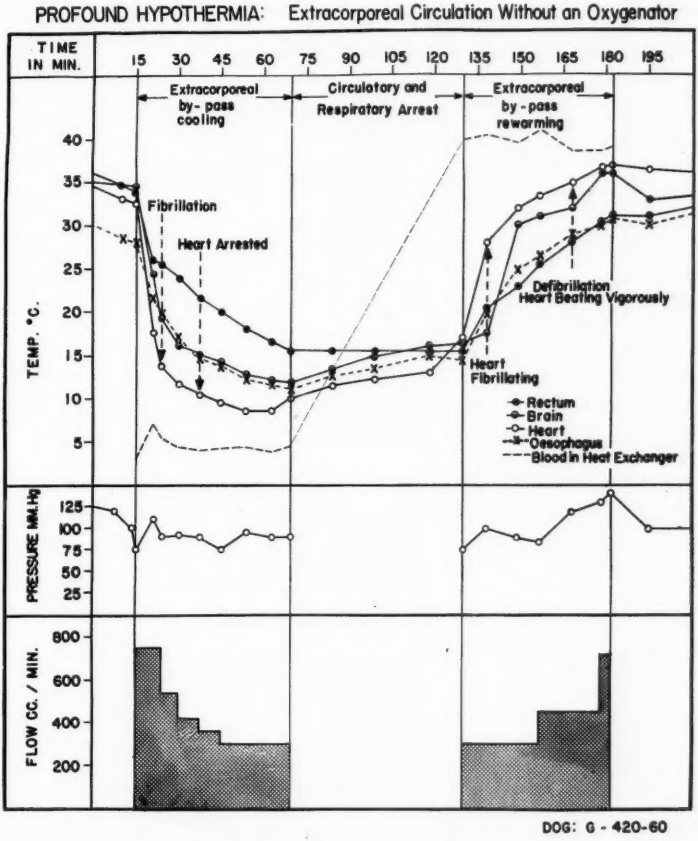

Fig. 5.—This figure represents the cooling and rewarming data from an animal of Group II.

TABLE III. THE VARIATIONS IN BLOOD FLOW AND PERFUSION PRESSURE DURING COOLING AND REWARMING IN THE ANIMALS OF GROUPS I AND II*

	BLOOD FLOW (C.C./KG./MIN.)		PERFUSION PRESSURE (MM. Hg)	
	MAXIMUM	MINIMUM	MAXIMUM	MINIMUM
		Group I		
Cooling	70	50	136	100
Rewarming	84	60	140	96
		Group II		
Cooling	45	28	120	50
Rewarming	60	34	130	40

*All data represent means values.

while brain, rectal, and muscle temperatures demonstrated a gradual rise. Warm perfusion was continued in all animals until rectal and brain temperatures were elevated to the range of 32° to 35° C. Termination of perfusion prior to this time invariably resulted in a hazardous fall of cardiac and esophageal temperatures toward the existing levels of rectal and brain temperatures.

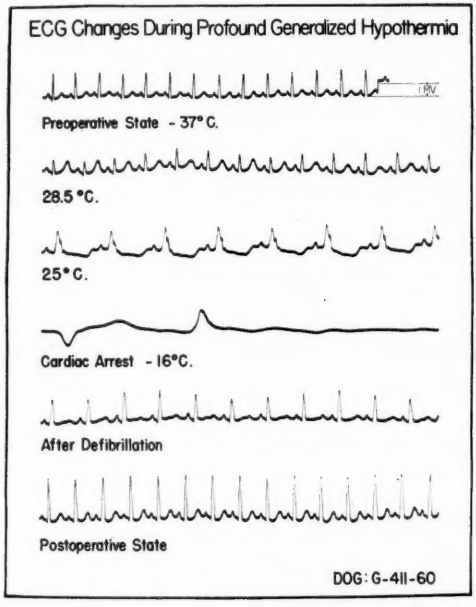

Fig. 6.—A reproduction of serial electrocardiographic tracings illustrating the physiologic changes which occur during cooling and rewarming.

TABLE IV. THE CORRELATION BETWEEN THE LOWEST VISCERAL TEMPERATURES AND THE DURATION OF HYPOTHERMIC AND TOTAL CIRCULATORY ARREST IN 10 REPRESENTATIVE ANIMALS OF GROUPS I AND II

NO.	LOWEST VISCERAL TEMP. (° C.)			DURATION OF HYPOTHERMIC CARDIAC ARREST (MIN.)	DURATION OF TOTAL CIRCULATORY ARREST (MIN.)	POSTOP. ECG AND EEG
	RECTUM	HEART	BRAIN			
				Group I		
1	13	8.5	8.5	55	33	Normal
2	11	7.0	8.0	74	60	Normal
3	15	9.5	11.0	38	28	Normal
4	12	7.5	11.1	58	43	Normal
5	15	10	10	40	31	Normal
				Group II		
6	14.5	15.0	15.0	53	34	Normal
7	16.5	9.5	15.5	53	30	Normal
8	18.0	15.0	19.2	48	25	Normal
9	15.0	10.0	12.0	87	60	Normal
10	18.5	10.0	13.3	67	48	Normal

B. Hypothermic Cardiac Arrest.—Initiation of high flow perfusion with pre-cooled blood in the animals of Group I resulted in rapid myocardial cooling and hypothermic arrest. This usually occurred during the first 5 minutes of perfusion at a mean temperature of 15° C. Ventricular fibrillation invariably preceded cardiac arrest, and developed at a mean temperature of 18° C. However, in several dogs, ventricular fibrillation was produced by the initial flush of cold blood through the coronary arteries. In all animals, the heart was in the

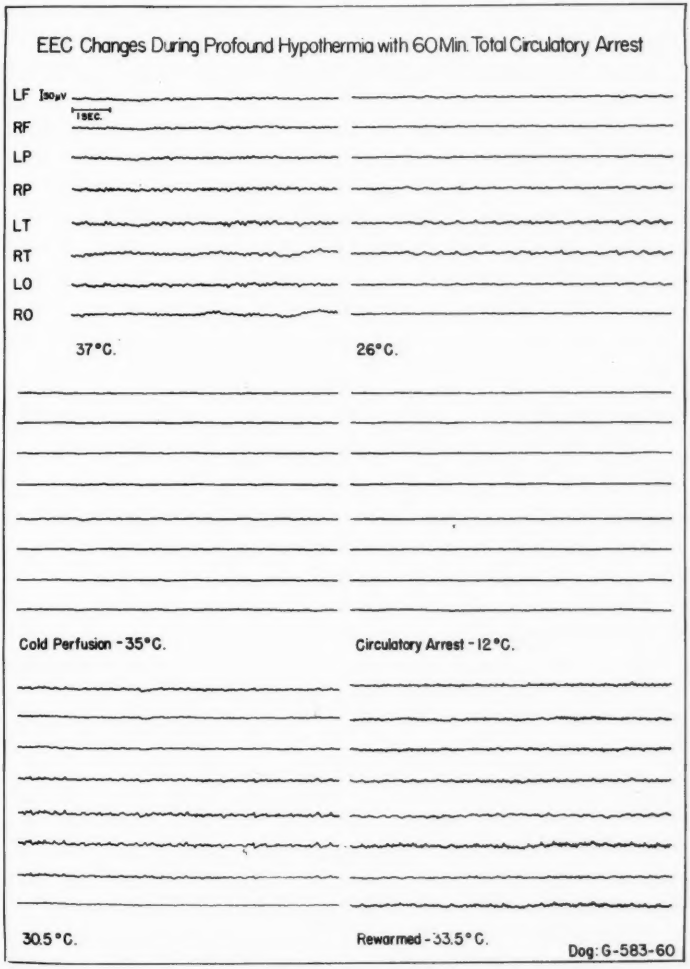

Fig. 7.—Electroencephalographic tracings are presented from an animal of Group I. The leads recorded electrical activity from the right and left frontal, parietal, temporal, and occipital areas. The initial flow of cold blood (2° C.) resulted in a temporary isoelectric tracing within 2 minutes (35° C.). Activity returned immediately, and persisted until 20° C. when the isoelectric state was again apparent. Rewarming of the brain after a 45-minute period of circulatory arrest (12° C.) was accompanied by a return of electrical activity.

arrested state during most of the cooling phase, and throughout the period of total circulatory arrest (38 to 87 min.; Table IV).

In the animals of Group II, there was a more gradual rate of myocardial cooling, and a delay in the onset of ventricular fibrillation and hypothermic cardiac arrest. However, ventricular fibrillation and cardiac arrest did occur in each animal at mean temperatures of 18° C. and 15° C. During the rewarming phase, reversion to normal sinus rhythm occurred spontaneously at a cardiac temperature of 30° C., or was produced by an electric shock of 130 volts.

C. Total Circulatory Arrest.—The 28 animals of the combined groups were subjected to single periods of circulatory arrest, varying from 25 to 60 minutes. Survival of animals after the 60-minute period of arrest occurred at temperatures of 8° to 12° C. (brain), and 11° to 15° C. (rectum) (Table IV). Post-rewarming electrocardiograms and electroencephalograms were interpreted as normal in all animals of the study. A further review of the effects of 60 to 120 minutes of circulatory arrest is underway.

D. Survival Data (Groups I and II).—Eight dogs included in the series died within the first 48 hours postoperatively. A large hemothorax was present in 6 animals, and 2 others were found to have a tension pneumothorax. No other abnormalities were noted. Twenty dogs who lived from 3 to 90 days were considered as survivors. There were no late deaths considered to be directly attributable to the hypothermia.

E. Electrocardiographic and Electroencephalographic Patterns During Cooling and Rewarming.—Profound hypothermia produced a marked alteration in cortical electrical activity. There was a rapid decrease in the amplitude of all frequencies during cooling, recorded in the frontal, parietal, temporal, and occipital leads. These changes were progressive until the isoelectric state was achieved (20° to 22° C.).[5, 6] Electrical activity returned to the pre-cooling level during the rewarming phase (Fig. 6).

The electrocardiographic changes which were observed have been described previously (Fig. 7).[1, 2] In general, bradycardia and varying degrees of heart block developed, and were followed by ventricular fibrillation and cardiac arrest. During rewarming, ventricular fibrillation again became apparent and was easily converted to a sinus rhythm at a cardiac temperature of 30° C.

DISCUSSION

The availability of prolonged, safe hypothermic cardiac arrest during cardiopulmonary bypass (Group I) appears to be an important adjunct to open-heart surgery on the basis of the following clinical considerations. (1) The cessation of rhythmic myocardial contractions which occurs during the initial few minutes of cold perfusion permits the repair of a tetralogy of Fallot or a ventricular septal defect in a quiet operative field. A reduction in coronary and bronchial arterial flow also takes place with cooling, and further facilitates the surgical procedure.[7, 8] (2) An operative approach to acquired or congenital lesions of the aortic valve would be possible (temperature range of 5° to 15° C.)

during a period of complete cessation of coronary circulation. With the proximal aorta cross-clamped, the previous hazard of rapid, spontaneous myocardial rewarming and subsequent cardiac hypoxia would be minimized by the associated reduction in temperature of all surrounding mediastinal structures. (3) The technical accomplishment of aortic arch replacement following resection of an aneurysm would be feasible during periods of total circulatory arrest.

As a consequence of the rapidity with which cardiac arrest developed in the animals of Group I, prompt decompression of the left side of the heart was a necessity. Failure to accomplish this decompression rapidly or effectively after commencing the bypass usually resulted in irreversible pulmonary congestion. The source of this relatively large blood flow into the left auricle and ventricle was believed to be the bronchial arteries.

In both groups of hypothermic animals studied, the depth of cooling was judged mainly by an appraisal of the rectal and brain temperatures. These parameters changed more gradually than the esophageal and cardiac temperatures, and seemed to reflect more closely the average or "core" temperature of the animal. This latter value was considered to be the temperature reached during the immediate post-cooling or rewarming period when an adjustment took place between the well-vascularized, parenchymatous organs and all other body tissues. Temperatures recorded from the mid-esophagus and myocardium during perfusion rapidly approached that of the perfusate, and so provided a false impression regarding the depth of the generalized hypothermia.

Profound hypothermia, produced during a left heart bypass (Group II), was a useful laboratory procedure but contained two disadvantages. First, the lower rate of blood flow inherent in the method resulted in a prolonged cooling phase. Second, there was a major dependence upon right ventricular contractions for an adequate pulmonary flow and so the attainable depth of cooling below 20° C. was often uncertain. However, the small priming volume of blood permitted by the elimination of an oxygenator from the system remained a valuable asset for the method.

SUMMARY

1. Profound levels of hypothermia were produced in 28 dogs utilizing two methods of perfusion:

a. In 16 animals (Group I), cooling was accomplished by incorporating a heat exchanger in the arterial line of a pump oxygenator unit. This method provided high blood flows and resulted in a rapid reduction of the visceral temperatures measured (esophagus, heart, brain, rectum, muscle).

b. Profound hypothermia was also produced in 12 dogs (Group II) by establishing a left heart bypass with a heat exchanger in the circuit. Low blood flows were obtained with this method and resulted in a slower rate of body cooling.

2. Prolonged periods of hypothermic cardiac arrest and total circulatory arrest were possible in both groups of animals with normal postoperative electro-

cardiograms and electroencephalograms.

3. The application of profound hypothermia, with or without total circulatory arrest, was suggested as an adjunct to the solution of certain clinical cardiovascular problems.

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THE MEMBRANE LUNG: AN IMPORTANT TECHNICAL IMPROVEMENT

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IN the modified Clowes lung, sealing is required along the outer edges of the membrane where it is provided by rubber gaskets compressed between two Plexiglas or metal plates with screw clamps. Sealing is also required for the membranes where they interdigitate with the blood distribution discs (Fig. 1).

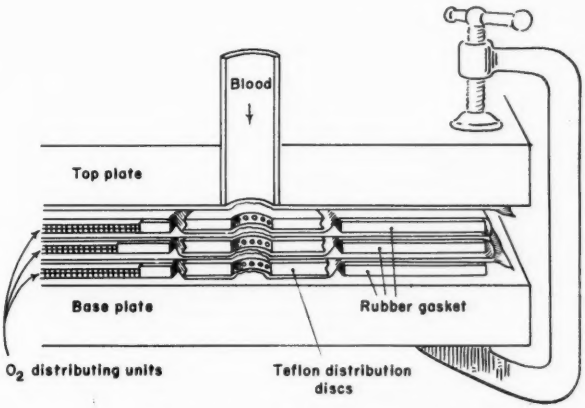

Fig. 1.—The way the membranes interdigitate with the blood distribution discs is illustrated. The thrust bearing may be mounted in the top plate or in the base plate to apply pressure to the Teflon distribution discs. When mounted in the top plate, the blood inlet or outlet is made in the base plate instead of the top plate. (From J. THORACIC SURG. 39: 438, 1960.)

Slight discrepancies in the thickness and composition of the blood distributing discs and the rubber gaskets have made it troublesome and sometimes quite time consuming to assemble the lungs without leakage. The problem has been solved by providing a separate way of applying pressure to the blood distributing discs by means of a thrust bearing (Fig. 2).

In use, the screw clamps are tightened first around the entire circumference of the lung. The thrust bearings are then tightened separately, using a special

From the Surgical Research Laboratory, East Tennessee Tuberculosis Hospital, the Department of Surgery, Acuff Clinic, and The Spinlab, Knoxville, Tenn..

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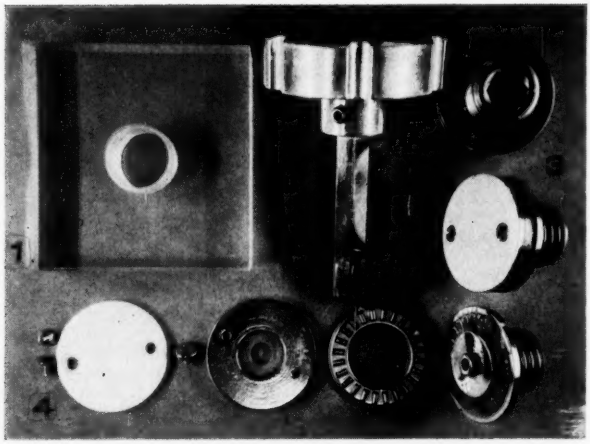

Fig. 2.—*1*, A Plexiglas plate for mounting the special thrust bearing. *2*, Hand wrench for tightening the bearing. *3*, Two assembled bearings. *4*, One disassembled bearing.

hand wrench which does not provide any excessive leverage; for, if the bearings are made too tight, there will be leakage between the rubber gaskets.

Lungs already built can easily be modified to incorporate the new thrust bearings. A small plate of Plexiglas or metal is drilled to fit the bearing. A 1½ inch hole is drilled in the top or bottom plate of the lung at each end to conform with the position of the blood inlet and outlet. The new bearing plate is centered over the hole and glued, welded, or bolted on.

Four previously constructed membrane lungs have been modified as described and several human total body perfusions have been performed successfully. A smaller versatile membrane lung, incorporating this improvement, is now being manufactured.*

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*The Spinlab, 312 Vine Avenue, Knoxville, Tenn.

CLOSED DRAINAGE OF POST-PNEUMONECTOMY EMPYEMA

L. Johansson, M.D., and G. William-Olsson, M.D., Stockholm, Sweden

THE TREATMENT of post-pneumonectomy therapy-resistant empyema often raises great problems. Drainage with or without suction, continuous flushing with antiseptic or antibiotic fluids, thoracoplasty, and total resection of the empyema cavity and thoracic wall have been tried.

Any form of therapy needs long hospitalization, but if the empyema cavity is continuously drained the patient feels quite well and can be sent home. Open drainage of empyema is very uncomfortable for the patients and, therefore, we have, in 2 cases, tried ambulatory treatment with closed pleural drainage, in which discharge from the pleura is gathered in a plastic bag. The bag,

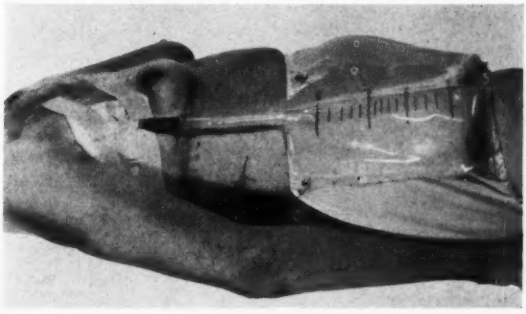

Fig. 1.—The appearance of the patient with the intercostal drainage connected to the bag.

when full, is changed by the patient. An intercostal drain is inserted in the subclavicular region and the tube dips into the deepest part of the pleural cavity. The exterior end of the tube is connected with a plastic bag into which, during coughing, the pleural contents empty (Fig. 1). This method has appeared to need very little control and has been quite comfortable for the patient. In 1 of the 2 cases in which the method has been used, obliteration of the empyema cavity has occurred after 8 months (Fig. 2, *A* and 2, *B*), and in the other case the cavity has diminished after a short period of treatment.

From the Clinic for Thoracic Surgery, Head: C. Crafoord, Karolinska Sjukhuset, Stockholm, Sweden.

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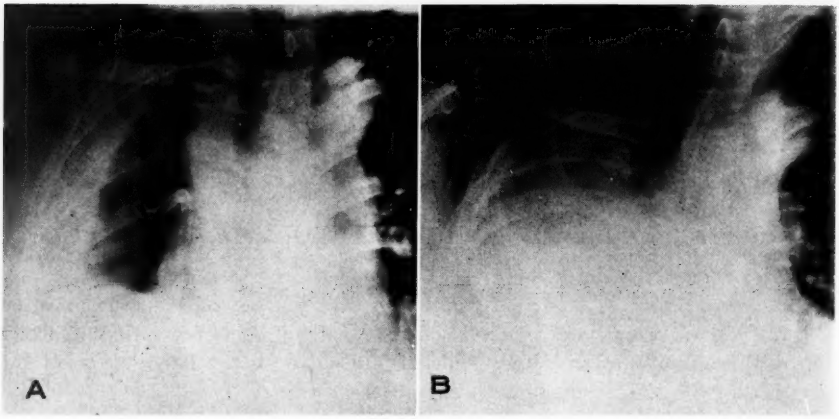

Fig. 2.—*A*, Roentgenogram of the empyema cavity during treatment. *B*, Roentgenogram after removal of the tube.

In a third patient with a late fistula in the incision of the chest wall, the tube was used for ambulatory treatment of a noninfected post-pneumonectomy pleural exudate. It was possible to remove the tube after a week without recurrence of the fistula.

SUMMARY

A simple method for closed ambulatory drainage of post-pneumonectomy empyema is presented.

Announcement

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Forty-second Annual Meeting of The American Association for Thoracic Surgery will be held April 16, 17, and 18, 1962, in St Louis, Missouri. Headquarters will be The Chase-Park Plaza Hotels.

Requests for Hotel Reservations

These should be mailed directly to Mr. T. J. Robinson, Executive Assistant Manager, The Chase-Park Plaza Hotels, St. Louis 8, Missouri. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1962 meeting *must be received on or before* **November 15, 1961,** otherwise they will not be considered by the Program Committee. These should contain *not more than* **200** *words* that accurately and clearly reflect the content of the completed paper. They should be labeled "For Thoracic Surgery Forum" or "For Regular Program," depending upon the nature of the subject matter. The Forum is primarily for the presentation of short papers on current thoracic research, experimental problems, anatomical studies, and modified or new surgical techniques.

Six, repeat, six clearly legible copies of each abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, Suite 311 Carondelet West, 7730 Carondelet Avenue, St. Louis 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting are to be published in the Journal and *must* be handed to the secretary *immediately* after their presentation. The maximum length allowed for Forum papers is 3,000 words without illustration. If illustrated, an appropriate number of words must be subtracted.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1961,** otherwise the application will be deferred for consideration until the 1963 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Charles K. Kirby, M.D.
Chairman of the Membership Committee
3400 Spruce Street
Philadelphia 4, Pennsylvania

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applications be held over for reconsideration a *second year.*